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RHEUMATIC PNEUMONIA

REPORT OF TWO CASES

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THAT rheumatic disease is the result of reaction to foreign antigens is a possibility that has been investigated for a number of years, and evidence for the anaphylactic genesis of the exudative lesions is steadily accumulating. Rich and Gregory[1] stated in 1943 that an allergic arthritis indistinguishable from rheumatic arthritis may occur in serum sickness, that the lesions in sulfonamide anaphylactic pneumonitis are histologically identical to those of rheumatic pneumonitis, and that the sharply focal lesions of periarteritis nodosa can be duplicated by injections of foreign antigen. The same authors, in a later paper,[2] say that egg albumen and horse serum, used as sensitizing agents, produce pulmonary lesions in rabbits similar to those seen in sulfonamide hypersensitivity and rheumatic fever. It has long been suspected that the specificity of the rheumatic response is dependent not so much upon the infecting organism as upon the individual mechanism of the rheumatic subject. A focus of infection in such an individual produces sensitivity rather than immunity of cells in other parts of the body. Analogously, in experimental animals, implants of *Streptococcus hemolyticus* result in a condition of allergy and extreme sensitization of cells far removed from the site of the organisms. If minute doses of antig are injected into the sensitized animal, an allergic reaction ensues which is manifested by severe, generalized edema.[3]

In addition to causing cellular sensitization, foreign antigens cause also the production of antibodies. If antigen and antibody meet in vascular tissue, the resulting reaction injures the previously sensitized endothelial cell of the capillary.[2] This mechanism could readily explain the recurrences of exudative features such as arthritic edema in persons with proliferative rheumatic lesions.[3-5] It may be also that streptococci render cardiac tissue antigenic in much the same way that they render kidney tissue antigenic in scarlet fever. Cavelti and Cavelti[6] have demonstrated in laboratory animals that the antigen (streptococci plus kidney tissue) causes the formation of autoantibodies which react with the antigen in renal capillary tufts to produce glomerulonephritis.

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Many investigators are of the opinion that the exudative lesions in rheumatic fever are likewise produced by this type of response to *Str. hemolyticus* infection.[3]

Pulmonic lesions in sulfonamide hypersensitivity, in anaphylaxis due to parenteral administration of foreign proteins, and perhaps in rheumatic fever, are due to focal endothelial cell injury with consequent increase in capillary permeability and transudation of albuminous fluid into the alveoli, alveolar ducts, alveolar septa, and interlobular spaces.[3-7] There is blood engorgement of the weakened alveolar capillaries, diapedesis of red blood cells into the alveoli, and infiltration of leucocytes into the alveoli and alveolar walls.[19] A severe anaphylactic reaction is seen in the cells of the septal wall as a focal cytoplasmic swelling with nuclear pyknosis and fragmentation. Necrosed septal walls rupture with resulting alveolar coalescence and intra-alveolar hemorrhage. If the endothelium of arterioles be damaged there is fibrinoid swelling of the arteriolar wall with polymorphonuclear and lymphocytic infiltration. This focal arteriolitis resembles the lesions of periarteritis nodosa.[1] Fibrinous and hyaline thrombi plug the ends of the ruptured vessels. The original albuminous transudate is pressed against the alveolar wall and, due to inspissation or to intra-alveolar air tension, becomes a hyaline membrane lining the alveoli and bronchioles.[5] Septal cells, or possibly the basal cells of bronchiolar epithelium,[8] proliferate to form a cellular lining of the alveolus and of the space formed by coalesced alveoli. These cells, assuming cuboidal shape, may form a single layer or they may be piled one on the other as a stratified cellular lining.[9] Many of them may contain hematogenic pigment. The plugs of fibrinous exudate which fill the alveolar ducts and project into alveolar spaces become organized and at first appear granulomatous, containing large spindle cells, mononucleated cells with abundant, pink-staining cytoplasm, pigmented macrophages, lymphocytes, and occasional erythrocytes. As organization proceeds, the plugs become fibrillary, with fibrin and fibroblasts arranged in layers like an onion. If the plug projects into and fills an alveolus lined with cuboidal cells, it appears to be covered by this layer of cells.[10] The completely organized plug consists only of dense fibrous tissue and may remain unchanged for an indefinite period, just as a healed Aschoff nodule may remain as a scar in the myocardium.[9] These plugs of organized exudate, sometimes called "Masson bodies," are probably cast or given specific shape by whatever mold, alveolar or ductal, that they happen to be in. There are often amorphous masses of organized exudate lying near by, which in no way differ from the Masson body in structural composition.[10] The pedicles of these plugs are attached to ductal or to septal walls and no doubt represent the route of invading fibroblasts in the process of organization. However, these plugs do not appear to connect with one another through the intra-alveolar pores as do the particles of organizing exudate in lobar pneumonia.[9] These peculiar, fibrous bodies are said to be present in bronchiectasis, tuberculosis, pulmonary abscess, and many other conditions in which focal intra-alveolar organization of blood or inspissated fibrin takes place.[10] Neubuerger and associates[9] view these Masson bodies, in part, at least, as granulomas

sprouting from the alveolar ducts, and the cuboidal alveolar lining as proliferated septal cells; whereas Herbut and Manges[10] and Herbut[8] insist that the bodies are organized, nonspecific exudate, and that the cuboidal cells are merely proliferated basal cells of the bronchiolar epithelium.

Since acute rheumatic fever is predominantly a childhood disease, and because most of the heart disease in children is rheumatic,[3] the possibility must be considered that the pneumonia which occasionally develops in a child with endocarditis is also rheumatic in origin.[11] Jensen[13] points out that probably many of the "primary atypical pneumonias" that have formerly been observed in cases of rheumatic fever were in reality rheumatic or poststreptococcic pneumonitis. Two cases of "atypical" pneumonia developing in the course of rheumatic fever are herewith presented.

CASE REPORTS

CASE 1.—A 7-year-old white girl, previously discharged from the Colorado General Hospital on Oct. 24, 1945, with a diagnosis of rheumatic heart disease, was readmitted, Jan. 17, 1946, with tachypnea and acute, postprandial, epigastric pain. There was no definite history of previous streptococcus infection. The patient was pale and apprehensive. Pulsations over the jugular veins were visible and palpable in the suprasternal notch, and a cardiac thrill was easily felt on the precordium. Heart rhythm was regular. A diastolic murmur was heard at the apex, and a mitral systolic souffle was transmitted to the left axilla. The red blood cell count was 4,270,000, the hemoglobin was 9.6 Gm. per cent, and the sedimentation rate was 57 mm. in sixty minutes with hemotocrit reading of 34 (Wintrobe). Platelet count, blood nonprotein nitrogen, plasma carbon-dioxide combining power, and urine were normal. Nose and throat cultures for *Str. hemolyticus* were negative. X-ray films of the chest showed congestive changes in both lungs and bilateral enlargement of the heart with the transverse diameter 2.5 cm. greater than on the previous admission. Electrocardiograms showed left ventricular strain. Despite absolute bed rest, high-vitamin, high-caloric diet, continuous oxygen inhalation, multiple blood transfusions, diuretic therapy, and digitalization, the clinical course was steadily downward to final expiration three weeks after admission.

Autopsy.—The autopsy was made seventeen hours after death. The unopened pericardial sac measured 14 cm. in diameter transversely, 13 cm. longitudinally, and 14 cm. obliquely through the apex. It was distended with 500 c.c. of fibrinous, straw-colored fluid with most of the fibrin settled posteriorly. The heart weighed 220 grams (twice average normal weight) and was pale and flabby. The epicardium was dull and covered with a thin film of fibrin. The thickened myocardium was pale but otherwise normal grossly. The endocardium was thick and wrinkled in the left auricle. Tricuspid, mitral, and aortic valvular cusps were opaque and showed numerous tiny, red, verrucose nodules on their apposing surfaces near the margins. The pulmonic cusps and all valve circumferences were normal. The left lung weighed 300 grams, the right, 430 grams (approximately three times average normal weight). They were mottled, bluish-purple, firm posteriorly, and irregularly crepitant anteriorly with slight elevation of the pink-yellow, crepitant areas above the surface of the firm portions. Multiple sections were flat and firm with very wet, dark red surfaces. The bronchial mucosa was hyperemic and the lumens contained frothy, blood-tinged fluid. Other organs appeared normal.

Microscopic examination.—The epicardium was thick with fibrous tissue, had a rough, fibrinous surface, and showed numerous small areas of fibrinoid degeneration invested by large mononuclear and multinuclear cells, which were in turn surrounded by lymphocytes and polymorphonuclears. In some places, fibroblastic proliferation was pronounced and collagen fibrils were very dense. Those subepicardial muscle fibers which were in contact with

the epicardial Aschoff body had either been replaced by connective tissue or showed cytoplasmic swelling and granulation with nuclear rhexis, pyknosis, or dissolution. The myocardium contained numerous Aschoff nodules. The lesions were focal, apparently in the arterial adventitia, and in the active phase of their production. There was no scarring, very little central necrosis of the nodule, and quite pronounced leucocytic infiltration. The endocardium (valvular cusps) was thick, fibrous, and contained lymphocytes, polymorphonuclear leucocytes, and diffusely scattered Aschoff cells that had made a slight attempt at palisading along the contact margin of the cusps. On some of the endocardial nodules there were degenerated masses of collagen, some of which pressed into the nodule while others appeared about to break away. Organisms could not be demonstrated.

The pleura was thickened with fibrous tissue and infiltrated mildly with lymphocytes. Alveolar walls were thick with proliferated septal cells and showed some hyalinization. In many places the wall projected as a knob of cells into the alveolus. Many alveolar walls showed necrosis and rupture with alveolar coalescense. The ruptured walls appeared to have contracted and presented bulbous ends plugged with pink-staining, collagenous material. Many alveoli were lined partially or completely with a single row of fusiform and cuboidal cells. These cells, slightly larger than lymphocytes, had definite fibrillary processes. Some of them contained particles of brown pigment. Apparently, the same cell became rounder, larger, and more burdened with pigment as it approached the center of the alveolus. Some alveoli contained blood and edema fluid; nearly all of them were packed with large, pigment-laden macrophages. Arteries in many places showed pronounced thickening of the adventitia on one side. In the center of this thickening was a cluster of large cells of the epithelioid type, some multinuclear, resembling Aschoff cells of the heart. Epithelium of the bronchi and bronchioles was normal.

The cortex and medulla of the cerebrum showed occasional, small, paravascular collections of lymphocytes.

Nothing remarkable was observed in other organs.

CASE 2.—A 9-year-old white boy was admitted to the Colorado General Hospital, Nov. 23, 1945, because of fever, anorexia, severe joint pains, and stabbing pains in the heart region. He first had these symptoms three weeks after a severe attack of scarlet fever in 1942, and since that time had had similar attacks nearly every month except during the summer. Between these episodes he had been symptom free. The boy was pale and undernourished. The pharynx was injected posteriorly, and cervical lymph nodes were enlarged. Examination of the heart elicited a precordial thrill, a loud systolic murmur, and a middiastolic murmur heard best at the apex. Hemoglobin was 12 Gm. per cent; the white blood count was 13,000 with 66 per cent polymorphonuclears. Urine was normal. Nose and throat cultures were negative for *Str. hemolyticus*. The patient was placed on absolute bed rest and supportive therapy. Signs of pulmonary disease developed. X-ray revealed heart enlargement and an extensive, mottled density of the right lung. Electrocardiograms showed slight right axis deviation. Continuous oxygen inhalation, intermittent penicillin and sulfadiazine administration, salicylization, and digitalization proved of no avail. Cardiac and pulmonary embarrassment progressed, anasarca developed, and the patient died three weeks after admission.

Autopsy.—The autopsy was performed nine hours after death. The peritoneum was smooth, glistening and contained 800 c.c. of clear amber fluid. The pericardium had a smooth, rather dull lining and contained 40 c.c. of fibrinous fluid. The heart weighed 290 grams (two and one-half times average normal), showed a dull epicardial surface, a pale, thick myocardium, and slightly shortened mitral cusps that had a row of firmly attached, pinhead-sized nodules on their apposing surfaces near the margins. The aortic valves were opaque but normal otherwise. Valve circumferences were within normal limits. The right lung weighed 470 grams (two and one-half times average normal), had a finely mottled surface, a purple-red color, a granularly firm consistence, and a peculiar, cut-surface mottling throughout. The firm, red areas appeared as small islands in the section surfaces. The left lung weighed 480 grams and presented gross features similar to those of the right lung.

Frothy, hemorrhagic fluid exuded from both bronchi. The brain, weighing 1,470 grams, showed mild edema, some leptomeningeal hyperemia, and slightly dilated ventricles full of clear fluid. Other organs appeared normal.

Microscopic examination.—Epicardial vessels were congested, and fibrous tissue was greatly increased. Subepicardial muscle cells were vacuolated. Many fibers were atrophied, and some were replaced with connective tissue which was abundant throughout. A few fibrosed, fusiform, Aschoff nodules dotted the myocardium. The endocardium was thick, fibrous, highly vascular, and contained collections of large, multinuclear cells. The bases of the mitral cusps were marked by extensive fibrosis, leucocytic infiltration (lymphocytes predominating), slight palisading of the Aschoff cells, interfibrillar vacuolization, and fibrin deposition on the surface.

The pleura was slightly thickened with fibrous connective tissue. Some alveoli were partially collapsed; some showed dilatation; others showed septum necrosis with rupture and alveolar coalescence. In some areas the alveoli were filled with blood and large vacuolated mononuclears, in others with mononuclears, lymphocytes, and polymorphonuclears, in still others with pigment-laden macrophages, polymorphonuclears, and edema fluid. Some of the alveolar walls were lined with hyaline membranes; others were thick and partially lined with several layers of septal cells. Emphysematous areas roughly alternated with areas of alveolar collapse and blood engorgement. Scattered throughout the lungs were variously shaped bundles of fibrous tissue which projected into alveoli from alveolar ducts. Cross sections of these bundles were, in the main, oval, round, or fusiform, and showed pronounced cellular polarity and whorl arrangement. Some were hollow and contained blood.

The meninges were thickened with fibrous tissue and contained small areas of necrosis partially surrounded by large flattened mononuclears, lymphocytes, plasma cells, and polymorphonuclear leucocytes. Arterial walls showed focal thickening and fibrosis with leucocytic infiltration and apparent vascularization in some places. Small, intracortical arteries showed adventitial thickening and tiny areas of fibrinoid degeneration surrounded by lymphocytes and large cells with abundant cytoplasm. Neuronal changes could not be demonstrated.

COMMENT

Some of the recent literature presents evidence which militates against rheumatic pneumonia as a disease entity. Much of it, however, not only supports the view that the pulmonary lesions are specific but also that they are allergic in their genesis and manifestations. By some investigators the Masson body is interpreted as an organized, nonspecific exudate; by others it is looked upon as a definite granuloma equivalent to the Aschoff body of the rheumatic heart.

According to the theory of allergenesis of exudative rheumatic pneumonitis, the antigens fabricated in the proliferative lesions of the heart circulate and sensitize cells of the pulmonary alveolar endothelium, and, in addition, bring about a gradual increase in humoral antibodies. When antibody titer is sufficiently high, the antigen-antibody reaction becomes violent enough to injure the sensitized cells. Resulting exudative lesions (as in the two cases reported) are seen in all phases of their production from slightly increased capillary permeability with edema, through endothelial necrosis and hemorrhage, to organization of the exudate and final fibrosis. In the first case, active proliferative lesions existed only in the heart. Exudative lesions were in the early active phase in the lungs and probably just beginning in the brain; death occurred before healing could begin. In the second case, proliferative lesions

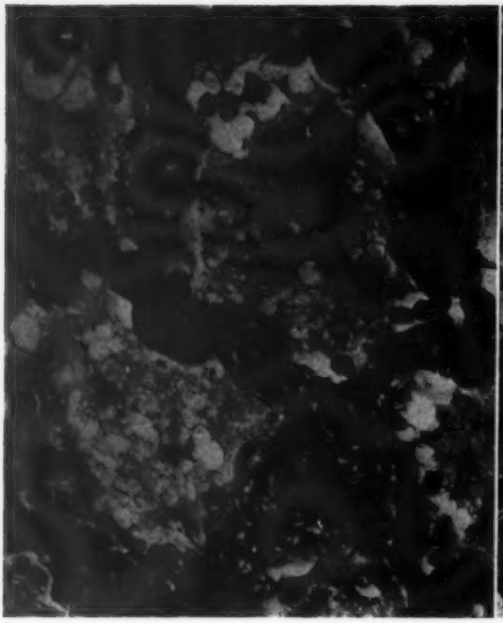

Fig. 1.

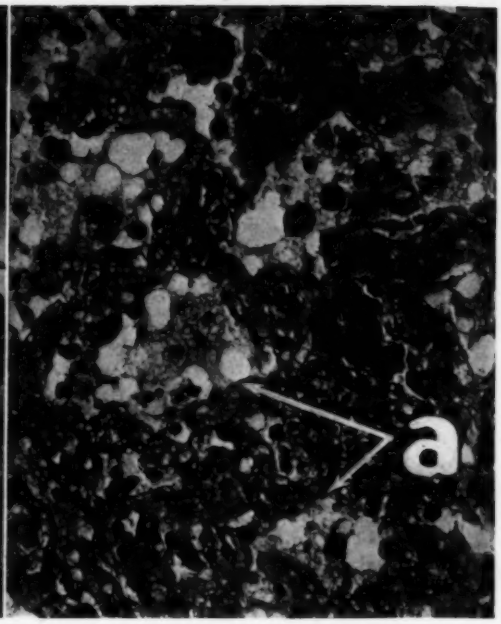

Fig. 2.

Fig. 1.—Section of lung (Case 1) showing septal wall congestion, alveolar transudate, and red blood cell diapedesis (*a*). ×450.

Fig. 2.—Section of lung (Case 1) showing septal cell proliferation and thickening of the alveolar wall (*a*). ×350.

Fig. 3.

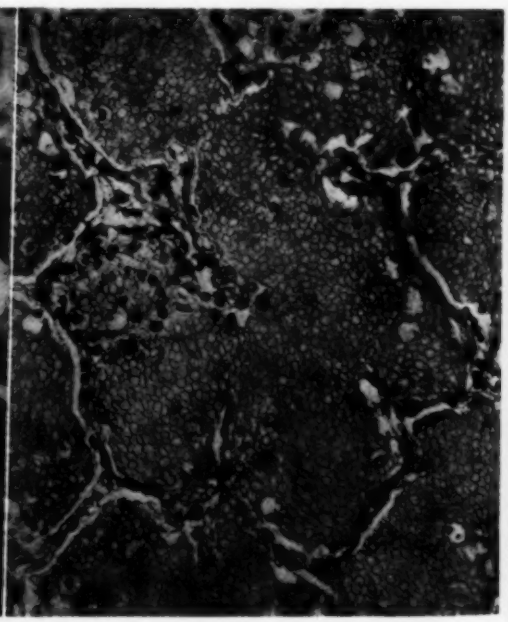

Fig. 4.

Fig. 3.—Section of lung (Case 1) showing mitotic figure in proliferating septal cell (*a*). ×970.

Fig. 4.—Section of lung (Case 1) showing rupture and collapse of septal walls with alveolar coalescence and hemorrhage. ×200.

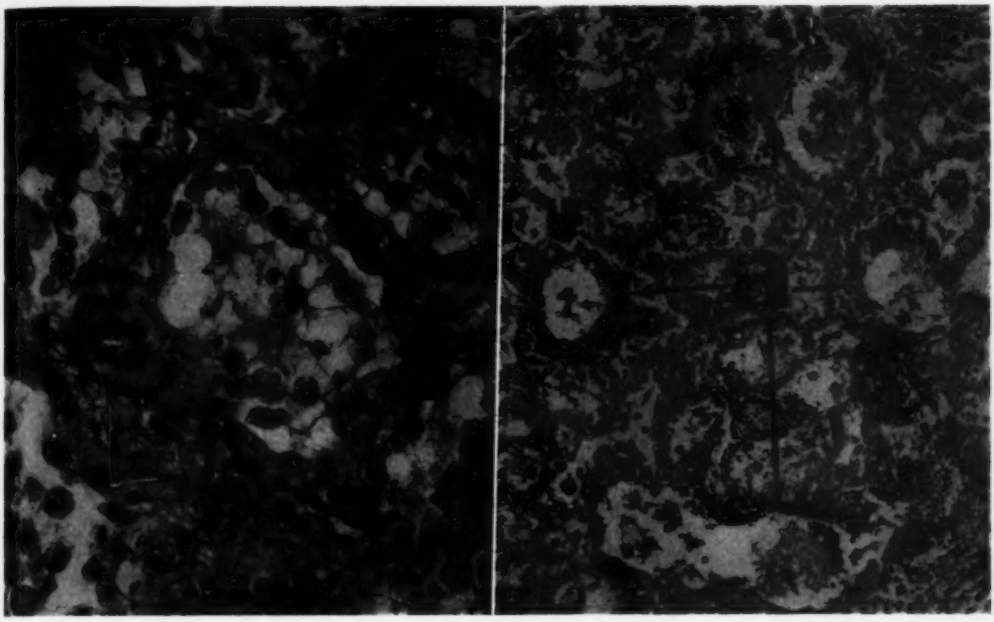

Fig. 5. Fig. 6.

Fig. 5.—Section of lung (Case 1) showing partial lining of alveolus with a single layer of cuboidal cells. ×450.

Fig. 6.—Section of lung (Case 1) showing several alveoli lined with hyaline membranes (*a*). ×150.

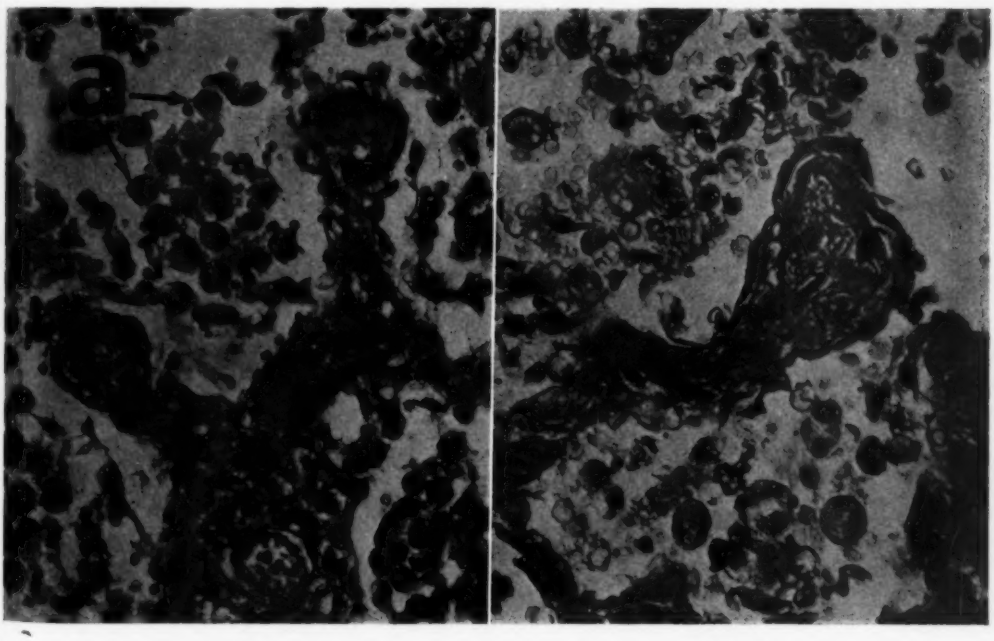

Fig. 7. Fig. 8.

Fig. 7.—Section of lung (Case 2) showing fibrinous plugs in ends of ruptured septa and alveolar infiltration with pigmented macrophages (*a*). ×450.

Fig. 8.—Section of lung (Case 2) showing an incipient Masson body with early fibroblastic investment of a particle of exudate. ×450.

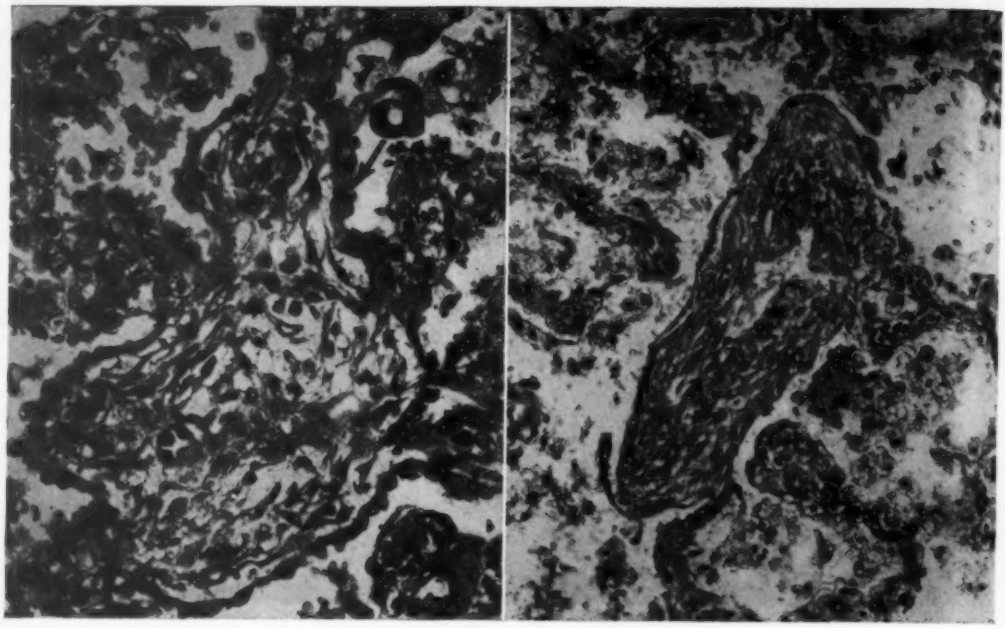

Fig. 9. Fig. 10.

Fig. 9.—Section of lung (Case 2) showing a granulomatous Masson body surrounded by a single layer of cuboidal cells (*a*). ×450.

Fig. 10.—Section of lung (Case 2) showing a fibrillary Masson body. ×350.

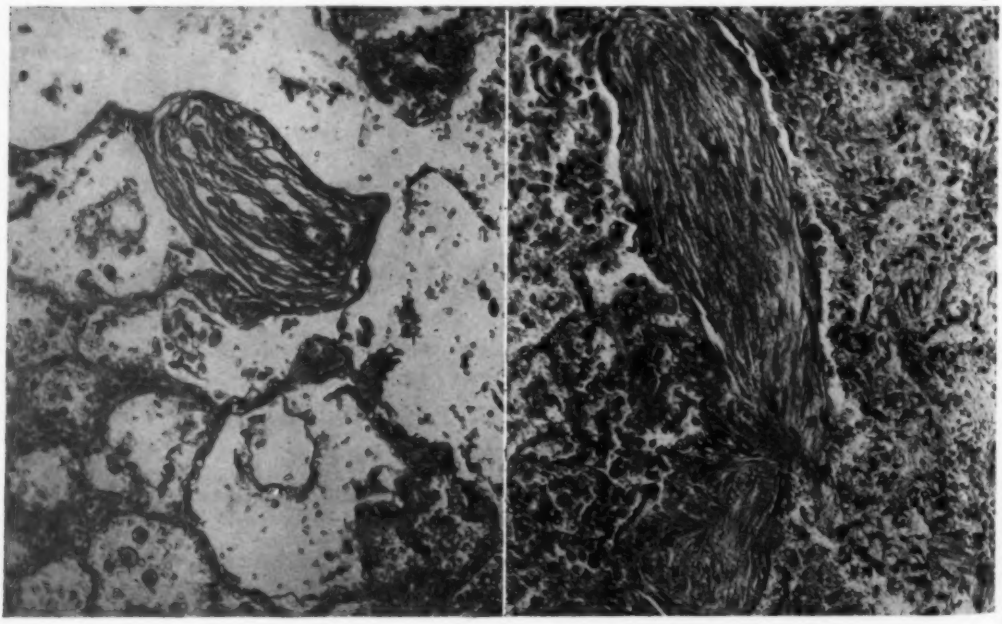

Fig. 11. Fig. 12.

Fig. 11.—Section of lung (Case 2) showing a Masson body with two septal attachments (pedicles) and pronounced cellular polarity and whorl arrangement. ×350.

Fig. 12.—Section of lung (Case 2) showing a fibrous Masson body. ×150.

of the heart were healing, exudative lesions of the lung and brain were clearing, and a few incipient proliferative lesions were appearing in adventitial connective tissue of the lung and brain.

The roster of supporters for the theory of specificity of rheumatic pulmonary lesions is increasing. Since Stoll[14] in 1788 spoke of rheumatic peripneunonia, others, including Garrod,[15] Paul,[16] Naish,[17] Masson and co-workers,[18] and Neubuerger and associates,[9] have accumulated evidence for such specificity. If the specific pulmonary lesion is anaphylactic in nature, as recent evidence seems to indicate, then the method of therapeutic attack in rheumatic fever will be altered considerably. It is not unlikely that rheumatic fever immunization, either active or passive, can some day be produced in the human being—a hope that may stimulate further investigation in this field.

Figs. 1 to 12 are microphotographs of the pulmonary lesions of the two patients whose cases are presented. These pictures portray in chronologic sequence the pathologic changes as they are generally understood in the dim light of present available information.

SUMMARY

Two new cases of so-called rheumatic pneumonia are presented. Together, these two cases of lung affection in children with rheumatic heart disease show most of the features of an exudative lesion resulting from injury to capillary endothelium. Pulmonary histopathology parallels that seen in experimental and sulfonamide anaphylactic pneumonitis.

The clinical histories of the two patients reported are consistent with the concept of an allergic mechanism in the production of pulmonary pathology and lay stress on the point that an exudative reaction such as pneumonitis may be delayed for some time after symptomatic subsidence of the initial endocarditis. This thought must be borne in mind in all cases of sulfonamide-penicillin-resistant pneumonia occurring in children with histories of rheumatic fever.

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HISTOPLASMOSIS IN INFANCY

Report of a Case in an Infant, With a Brief Clinicopathologic Review

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IN 1906, Darling reported the first case of histoplasmosis, from the Panama Canal Zone. In this report and in his two succeeding reports in 1908 and 1909, he stated that he regarded the etiologic organism to be a protozoan similar to the genus Leishmania. It was not until 1921 that Rocha-Lima first suggested, and not until 1934 that de Monbreun definitely established that the organism is a fungus of the genus Posadasia. In tissues, the organism exists as a thick, encapsulated yeast cell, 1 to 5 microns in diameter. It is usually found in the large, mononuclear, reticuloendothelial cells.

Since Darling's first article, eighty-eight cases of histoplasmosis have been reported. In twenty-eight of these, the patients were children. Twenty were infants less than 15 months of age. Because in few of these cases was histoplasmosis diagnosed clinically and because the present case has some interesting features, a report in conjunction with a short review of the clinicopathologic picture in infants may be of value.

CLINICOPATHOLOGIC REVIEW

Of the eighty-eight cases in the literature, the distribution has been world wide. The majority of the cases however, have come from the Mississippi River basin, where the disease is apparently endemic. As was stressed in an article by Iams and associates,[1] the clinical picture presented in infants is quite different from that in adults. As the case reported in this paper will illustrate, the usual clinical findings in an infant consist of fever, loss of weight, chronic cough, and diarrhea, associated with hepatosplenomegaly, lymphadenopathy, hypochromic normocytic anemia, and leucopenia. If a patient presents all of the findings in Group A, Table I and one or more of the findings in Group B, Table I, histoplasmosis should be considered a definite possibility.

Table I. Clinical Findings in Histoplasmosis of Infants*

GROUP A	GROUP B
Fever and loss of weight	Leucopenia or normal leucocyte count
Hypochromic normocytic anemia	Lower respiratory infection
Splenomegaly	Gastroenteritis
Hepatomegaly	Lymphadenopathy
	Dermatitis
	Upper respiratory infection

*Arranged in order of frequency in twenty reported cases.

Pathologically, the fungus involves, in order of frequency, the lungs, lymph nodes, liver, spleen, gastrointestinal tract, bone marrow, adrenal glands, thymus, skin, pancreas, myocardium, kidneys, and brain (Table II).

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TABLE II. SITES OF PATHOLOGIC FINDINGS IN HISTOPLASMOSIS OF INFANTS*

GROUP A	GROUP B
Lungs	Bone marrow
Lymph nodes	Adrenal glands
Liver	Thymus
Spleen	Skin, pancreas, myocardium, etc.
Gastrointestinal tract	

*Arranged in order of frequency in twenty reported cases.

Diagnosis.—In infants and children as well as in adults, there are several disease processes with which histoplasmosis might be confused. Because of the hepatosplenomegaly and lymphadenopathy, the lymphoblastomatous diseases must be ruled out. These diseases might present all of the clinical findings in Group A and several of the clinical findings of Group B (Table I) and thereby satisfy the requirements for a clinical suspicion of histoplasmosis. Blood studies and biopsy of a lymph node or bone marrow will usually show the characteristic pathologic pictures of these diseases.

In cases of tuberculosis, all or most of the clinical findings of Group A and part of Group B might also be present. The roentgenographic findings in the thorax in the two diseases are quite similar and may further confuse the picture. The diagnosis could best be made by the diagnostic methods used in tuberculosis or by sternal biopsy.

Pancreatic cystic fibrosis might also offer some difficulties in differentiation. Chronic cough, loss of weight, anemia, diarrhea, and fever are observed in both diseases. Also, the roentgenologic findings might be quite similar. However, hepatosplenomegaly is not commonly observed in pancreatic fibrosis. The diagnostic laboratory studies used in each of these diseases are adequate to enable one to make a final decision.

Erythroblastosis foetalis and congenital syphilis may present some of the clinical findings of histoplasmosis. Blood Wassermann reactions and Rh factor studies of the parents and infant will usually serve to differentiate these diseases.

The diagnostic procedures used in histoplasmosis are biopsy of bone marrow, liver, and spleen, thick blood smears, blood cultures, and intradermal tests with histoplasmin.[2] The most dependable of these methods is biopsy of the bone marrow or one of the organs.

Prognosis.—The prognosis as far as has been determined at the present time is uniformly poor. In all but one case reported to date the patient has died.

CASE REPORT

The patient, a female infant, was born in Illinois on April 7, 1945, after a full forty weeks' gestation. Her mother, thirty-five years of age, father, forty-one years of age, and a sibling, three years of age, are all living and in good health. The infant weighed 7 pounds, 8 ounces (3.40 kilogram) at birth, gained well on formula feedings, and was in normal health until June, 1945. At the age of 2 months she was seen by the family physician because of fussiness, irritability, and sleeplessness. She was found to be moderately anemic and responded well to iron therapy.

The infant remained apparently well until October, 1945, when, at 6 months of age, she was again taken to her family physician because of icterus, pallor, and a temperature of 103° F. At this time hepatomegaly was first noted and a diagnosis of hepatitis was made.

Her general condition became worse and on November 9, râles and decreased breath sounds were noted on the left side of the thorax posteriorly. A large spleen was also found. The concentration of hemoglobin was 7.5 Gm. per 100 c.c. of blood; erythrocytes numbered 2,760,000 and leucocytes 3,900 per cubic millimeter of blood, with lymphocytes 41 per cent and polymorphonuclears 59 per cent. The cerebrospinal fluid showed three lymphocytes but was otherwise negative. A roentgenogram of the thorax was negative. The patient's temperature continued elevated between 103° and 104° F. A diagnosis of atypical pneumonia with associated aplastic anemia was made and the patient was treated with whole blood transfusions, sulfonamides, and penicillin.

Fig. 1.—Infant with liver and spleen demarcated.

On Nov. 13, 1945, at the age of 7 months, the patient was referred to the Mayo Clinic and was admitted to a hospital for further study and treatment.

The physical examination on admission to the hospital showed a well-nourished, well-developed, moderately pale infant, appearing chronically ill. Her rectal temperature was 101.5° F. The liver and spleen were enlarged five centimeters below the costal margins (Fig. 1). There were no other abnormal physical findings. She weighed 18 pounds (8.15 kilograms).

At this time the concentration of hemoglobin was 12.6 Gm. per 100 c.c. of blood; erythrocytes numbered 3,640,000 and leucocytes, 1,900 per cubic millimeter of blood. Urinalysis showed no abnormalities. There was no increased fragility of the erythrocytes. No plasmodia were found in a thick smear. Blood smears showed hypochromic, macrocytic anemia with increased regeneration, occasional basophilic stippling, and toxic granules in the polymorphonuclear cells. The flocculation reaction for syphilis was negative. The concentra-

tion of the serum bilirubin both direct and indirect was within the normal range. The sulfobromophthalein liver function test showed retention of the dye, grade 1 (on the basis of 1 to 4, in which 1 designates the least and 4 the greatest retention). The cephalin flocculation reaction was positive. The prothrombin time (Quick's test) was 19 seconds (normal). The concentration of proteins was 5.8 Gm. per 100 c.c. of serum with an albumin-globulin ratio of 3.06:1. Roentgenograms of the thorax, head, and long bones were all normal. Blood cultures taken at this time were reported negative in forty-eight hours.

The patient's course was stormy during hospitalization. The rectal temperature curve ranged from 99.6° to 104.0° F. each day, with peaks at 8:00 A.M. and 8:00 P.M. This type of curve persisted until she died. She lost weight rapidly, and on November 19, weighed 7.62 kilograms, 0.53 kilogram less than on admission.

On November 22, administration of 10,000 units of penicillin every three hours was begun. This was continued for only eighty-four hours, the patient having received 240,000 units in all. Penicillin was of no apparent value to the patient. At this time, the concentration of hemoglobin was 8.25 Gm. per 100 c.c. of blood; erythrocytes numbered 2,710,000 and leucocytes 1,100 per cubic millimeter of blood. Numerous differential counts of the leucocytes revealed neutrocytosis with a shift to the left. Seven transfusions of citrated whole blood (60 to 75 c.c. each) were given on alternate days. However, they were of only momentary value, for the profound anemia became even more severe. On December 10, laboratory studies showed 2,150,000 erythrocytes per cubic millimeter of blood and 7.3 Gm. of hemoglobin per 100 c.c. of blood.

Because of the history, physical findings, hypochromia, macrocytic anemia, and leucopenia, histoplasmosis was suspected, and a biopsy of bone marrow was done on Nov. 23, 1945, by Dr. Hargraves of the Division of Medicine, Mayo Clinic. His report is as follows:

"A satisfactory bone marrow preparation was obtained by tibial puncture. There were some units present. Smears were made in the usual fashion and stained with Wright's stain. Examination of the smears showed moderate cellularity present with the usual myeloid-erythroid ratio. There were some basophilic normoblasts and pronormoblasts but most of the normoblasts were late polychromatophilic cells. In the myeloid line there were numerous older forms with about a normal age dispersion of the immature forms. Most of the mature neutrophiles were vacuolated and appeared to be degenerating forms. In the cytoplasmic vacuoles of many of these cells were inclusion bodies about the size of platelets, many showed a sharply defined capsule and there was a central mass of chromatin which was rather smooth and dark.

"An occasional monocyte was found with multiple organisms in a large vacuole. There were many large phagocytic reticuloendothelial cells with these same organisms contained in their cytoplasm—some having as many as twenty present. One eosinophile was seen containing two parasites, and an occasional megakaryocyte was also parasitized. Interestingly enough, I was unable to find them in any of the immature forms, either myeloid or erythroid, and no lymphocytes were seen parasitized. This would suggest that the parasites were phagocytized by the mature cells. There were many free organisms found around clumps of cells and strung out alone in some fields. These were undoubtedly *Histoplasma capsulatum* (Histoplasmosis of Darling)." Figs. 2 to 6 show the organism.

At this time, histoplasmin dermal tests were applied to both of the infant's forearms in dilutions of 1:1,000, 1:500, 1:100, and 1:10, with proper controls, and the tests were repeated three days later, with no reaction in forty-eight or seventy-two hours. A dermal test was also applied to the forearm of the patient's mother. In forty-eight hours the erythematous area of the histoplasmin test on the patient's mother measured 5.4 by 3.6 cm. The erythematous area of the control reaction measured 2.4 by 1.6 cm. This was considered a positive reaction.

Soon after the diagnosis of histoplasmosis had been made by means of the bone marrow biopsy, specific treatment was attempted. To date, the only specific therapeutic agent mentioned in the literature is Neostam (nitrogen glucosides of sodium paraminophenyl stibonate). This was given intramuscularly to the patient in doses of 0.001 Gm. per pound of body

Fig. 2.

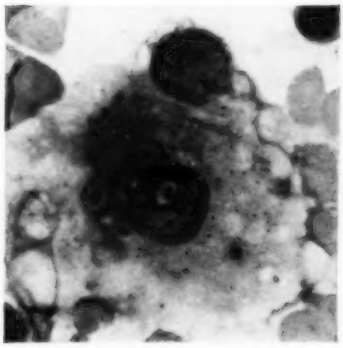
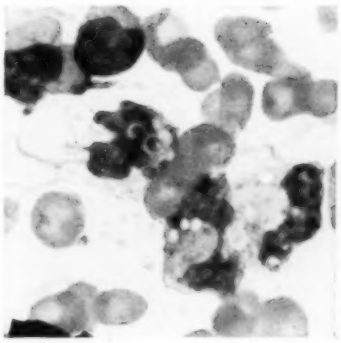


Fig. 3.

Fig. 4.



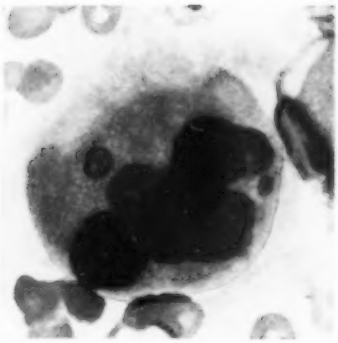


Fig. 5.

Fig. 2.—Bone marrow showing *Histoplasma capsulatum* in a reticuloendothelial cell (Wright's stain, ×1,000; section made by Dr. M. M. Hargraves).

Fig. 3.—Organisms in monocyte (Wright's stain, ×1,000; section made by Dr. M. M. Hargraves).

Fig. 4.—Organisms in polymorphonuclear leucocyte (Wright's stain, ×1,000; section made by Dr. M. M. Hargraves).

Fig. 5.—Organisms in megakaryocyte (Wright's stain, ×1,000; section made by Dr. M. M. Hargraves).

Fig. 6.—Organisms in eosinophile (Wright's stain, ×1,000; section made by Dr. M. M. Hargraves).

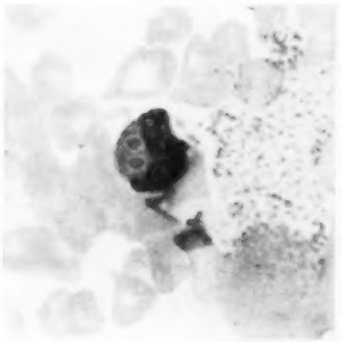


Fig. 6.

weight, amounting to 0.01 Gm. per day on December 12 and 14. This seemed to have no influence one way or another. The blood cultures that had been taken previously were reported in ten days as showing many colonies of *Histoplasma capsulatum*. Cultures of the sternal marrow also gave positive results. Stools were cultured on plates of hormone blood agar with 20 units of streptomycin added as described by Thompson,[3] and colonies of *Histoplasma capsulatum* grew out. Secretions from the duodenum were obtained by tube and cultured at room temperature in like manner and also showed growth of *Histoplasma capsulatum* in twenty days. Repeated cultures of the urine were all negative.

The infant's condition became progressively worse. Tube feeding was necessary for the last two weeks of the patient's life because of anorexia and weakness. On December 15, she became very listless, cyanotic, and dyspneic, and petechial hemorrhages appeared on the trunk. She was placed in an oxygen tent. The following day edema of the lower extremities were first noted. She began vomiting all her feedings, respirations became more rapid, and she died.

Because of the positive reaction to the histoplasmin dermal test, the patient's mother was examined for any signs of latent histoplasmosis. Physical examination was entirely negative with the exception of two involuting macules on the right breast which represented previous draining pustules. The concentration of hemoglobin was 13.5 Gm. per 100 c.c. of blood; erythrocytes numbered 4,220,000 and leucocytes 9,000 per cubic millimeter of blood, with lymphocytes 29 per cent, monocytes 3, polymorphonuclears 66, eosinophiles 1, and basophiles 1 per cent. The flocculation reaction for syphilis was negative. The erythrocyte sedimentation rate (Westergren) was 28 mm. per hour. A roentgenogram of the thorax was normal. No signs of histoplasmosis could be found.

Necropsy.—Necropsy revealed the typical pathologic picture of the disease. The heart, lungs, liver, spleen, kidneys, adrenals, esophagus, large bowel, urinary bladder, lymph nodes, thymus, bone marrow, and diaphragm, were all found to be invaded by the organism.

The organism was cultured from the blood, lungs, liver, spleen, kidneys, bone marrow, rectus abdominis muscle, and frontal lobe of the brain.

The pathologic and bacteriologic findings will be published in full elsewhere.[4]

COMMENT

There are several interesting factors in this case. It is one of the few cases in the literature in which the diagnosis was made ante mortem. This was accomplished primarily by considering the disease as a possibility because of the clinical picture. This led to a biopsy of bone marrow revealing the organism.

In our case, the organism was cultured for the first time from the stools, duodenal drainage, and urine. This gives evidence of the infectiousness of histoplasmosis and adds some facts to the still vague epidemiological picture of the disease.

The reactions to the intradermal tests were particularly interesting but definite interpretation is lacking. The negative reaction of the infant duplicates previous experience at the Mayo Clinic in an unreported case. This reaction may be considered comparable to that seen with tuberculin in miliary tuberculosis. This, however, is not the experience of several authors in the literature.[5-7] The positive reaction of the patient's mother, with no evidence of histoplasmosis, is interesting but also without any adequate explanation. One might postulate the presence of a previous or latent infection with a possible intrauterine invasion of the infant. However, Emmons and his associates[8] have shown the lack of specificity of the histoplasmin intradermal test in particular and fungus intradermal tests in general. They studied antigens prepared from cultures of

Histoplasma capsulatum, Blastomyces dermatitidis, Coccidioides immitis and *Haplosporangium parvum*. Cross reactions were demonstrated between all four antigens. A positive reaction to 1:100 histoplasmin was shown in guinea pigs, experimentally infected separately with histoplasmosis, blastomycosis, coccidioidomycosis or haplomycosis. Positive reactions were found in patients to both histoplasmin and blastomycin. The possibility of a latent, low-grade histoplasmosis, leaving the patients perfectly well but showing calcified hilar nodes and a positive histoplasmin intradermal reaction, has been postulated by Palmer.[9] The studies of Emmons and his associates cast a shadow of doubt on these postulations but further study is indicated.

SUMMARY

A case of histoplasmosis in an infant is reported, with a brief review of the clinical and pathologic picture. This report is distinctive in that the organism was cultured for the first time ante mortem from the stool, urine, and duodenal drainage.

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SALICYLATE INTOXICATION IN THE INFANT AND YOUNG CHILD

A Report of Thirteen Cases

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SPORADIC cases of salicylate intoxication have been seen at the St. Louis Children's Hospital in the past.[1] During the period of October, 1944, to June, 1946, there were thirteen patients with salicylate intoxication admitted to the hospital. Most of these patients were infants who received aspirin as treatment for a "cold." In only two instances was accidental ingestion of medication reported. The danger of salicylate poisoning cannot be overemphasized to parents or physicians who administer salicylate to children, and especially to infants. This danger obviously is intensified when salicylates are given over a period of several days or in large doses. Case reports in the literature of salicylate intoxication have increased during the past year. This report represents the largest group of patients with salicylate intoxication admitted for hospital care. A similar pattern of acid-base imbalance was noted in all of these patients, and this response is presented as that typical of salicylate intoxication in the infant and young child.

METHODS

In each of the thirteen cases reported, studies included salicylate concentration of the blood plasma and spinal fluid,* pH of the blood serum by the method of Hastings and Sendroy,[3] carbon dioxide content of the serum,[4] prothrombin time by the method of Ziffern and associates,[5] and urine examination. Other laboratory studies included serum chloride, glucose, and nonprotein nitrogen determinations. Blood ketone body studies[6] were made in two cases. A large vein was selected for venipuncture (usually the femoral vein), and the blood was obtained carefully in a chemically clean and sterile syringe, and placed immediately under paraffin oil so as to avoid changes in pH and carbon dioxide. Therapy was instituted immediately after the blood samples were taken because of the severe state of collapse noted in most of these patients. An attempt was made to determine the amount of salicylate administered to or accidentally ingested by the patient. In most instances, information was obtained by questioning the parents and the pharmacist filling the prescription.

ANALYSIS OF CASES

Age, Sex, and Race.—The ages of the patients ranged from 3 weeks to 3½ years. There were six girls and seven boys; most of the younger patients were boys. All of the children were white except two Negro siblings.

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*The method of Brodie and associates[2] was employed for these determinations, and the results were expressed in milligrams per 100 c.c. For comparison with other reports in the literature, 1.0 gamma per c.c. is equivalent to 0.1 mg. per 100 c.c.

TABLE I. SYMPTOMS AND SIGNS NOTED IN CASES OF SALICYLATE INTOXICATION

CASE	AGE	SALICYLATE RECEIVED	SYMPTOMS AND SIGNS	TEMPERATURE ON ADMISSION (°C.)	TOTAL WBC
1	3 wk.	22½ grains in 2 days (aspirin)	Cold with cough, 4 days (aspirin started 3½ days before entry); deep, pauseless breathing, 2½ days; attacks of cyanosis, 2 days (aspirin discontinued 24 hr. before entry); moderate dehydration	39.5	10,100
2	6 mo.	27 grains in 1 day (aspirin)	Deep, pauseless breathing, 24 hr. (beginning about time aspirin was started but increasing during that period); slight dehydration; listlessness; color of skin gray; pharynx reddened	38.5	9,150
3	26 mo.	15 grains in 2 days (aspirin)	Cough, 4 days (aspirin started 4 days before entry); vomiting, 3 days; deep, pauseless breathing, 2 days (aspirin discontinued 1½ days before entry); listlessness, 2 days; semistuporous on entry; moderate dehydration; acute rhinopharyngitis and bronchitis	38.5	12,800
4	8 mo.	Yellow pills (?) 8 daily for 4 days	Fever and cold 5 days ("yellow pills" started 4 days before entry); vomiting 2-3 days before entry (medication discontinued before entry); deep, pauseless, and rapid breathing, 24 hr.; listlessness, 24 hr.; slight dehydration and cyanosis; acute, serous otitis media, right; right sixth cranial nerve palsy; convulsions 1-3 days after entry to hospital	39.5	19,600
5	4½ mo.	60 grains in 3½ days (aspirin)	Cold, 1 week (aspirin started 3½ days before entry; fever, 3 days; anorexia and vomiting, 3 days; deep pauseless respiration, 1 day; stuporous, 4 hours; convulsive twitching, 3 hours; comatose on entry; moderate dehydration; rhinopharyngitis, bronchitis, acute catarrhal otitis media bilateral	40.0	11,300
6	3½ mo.	10-15 grains per day (mother vague and reluctant in giving dosage of aspirin)	Cold, 1 week (aspirin given frequently by mother, dosage vague, patient had at least 10-15 grains in 24 hr. prior to entry); deep, pauseless breathing 18 hr.; listlessness, 18 hr.; comatose on entry; skin ashen gray in color; moderate dehydration; acute rhinopharyngitis	38.5	17,000
7	2½ yr.	45 grains in 2 days (aspirin)	Cold, 5 days (aspirin begun 2 days before entry); deep, pauseless breathing, 12 hr.; vomited 1 or 2 times 2 hr. before entry; pallor (but did not appear severely ill, no manifestation of dehydration); tonsillitis and pharyngitis, subacute	39.2	11,800

TABLE I—CONT'D

CASE	AGE	SALICYLATE RECEIVED	SYMPTOMS AND SIGNS	TEMPERATURE ON ADMISSION (°C.)	TOTAL WBC
8	20 mo.	8 tsp. daily; unknown medication for 2½ days	Fever, 4 days; cold (unknown medication for 2½ days); twitching 12 hr. before entry; deep pauseless respiration, moderate; acute otitis media, right ear	40.0	7,200
9	5 mo.	30-60 grains in 3 days (aspirin)	Cold, 1 week; fever, 3 days (aspirin started 3 days before entry, ¼-½ tablet every 3 hr.); restlessness and irritability, 8 hr.; hyperpnea, 8 hr.; listless and drowsy on entry; rhinopharyngitis and tonsillitis; petechiae over chest; bloody emesis, 20 c.c.	37.7	9,300
10	2 yr.	126 grains in 3 days (aspirin)	Upper respiratory infection, 3 days (A.P.C. tablets every 2 hr. for 3 days); hyperpnea 1 day before entry and continued 24 hr. after entry and treatment	38.0	14,000
11	21 mo.	Accidental consumption of unknown amount of liniment	Hyperpnea; listlessness; moderate dehydration	37.5	17,100
12	3 yr.	Same as above (siblings)	Hyperpnea, slight; disorientation, slight; ataxia, slight	37.0	10,000
13	3½ yr.	24 grains of aspirin in 2 days	Headache, fever, vomiting, 6 days; sore throat, 3 days; listlessness, 3 days; hyperpnea, slight (noted on admission); tonsillitis	37.8	7,000

History of Present Illness.—The patients were admitted with a history of "cold" and, in some instances, cough for from four to seven days. All of them had received salicylates (definitely known to be aspirin in eleven cases) in large dosages for at least one to four days prior to admission. Liniment containing salicylate was accidentally ingested by two Negro siblings. Abnormal breathing was noted by the parents and described as deep and pauseless. This abnormality in respiration was seen from eight to sixty hours before hospitalization, and either accompanying or, more often, following the onset of this change in respiration, there was listlessness which rapidly became more pronounced. Vomiting occurred in five of the patients in addition to marked anorexia. This decrease in caloric and liquid intake continued for as long as three days prior to entry.

Clinical Findings.—The appearance of the patients was that of ill or severely toxic infants or young children. Although no temperatures were taken by parents, rectal temperatures of nine of these patients varied between 38 and 40° C. on admission. All of the patients were either very pale or cyanotic; most were slightly or moderately dehydrated and apathetic; the younger and smaller ones were more often semicomatose or stuporous. All manifested abnormal respiration. Respirations were exaggerated in depth and followed one another with little or no intervening pause.

The youngest and smallest patient of this series (Case 1, Table I) demonstrated hemorrhagic tendencies manifested by epistaxis, tarry stools, and xanthochromia of the spinal fluid. The aspirin was administered approximately three and one-half days before entry, and the bleeding tendencies were noted within the first day of hospitalization. The prothrombin time was prolonged.

One of the patients had generalized convulsions during the first three days of hospitalization; two others developed mild twitchings three and twelve hours before admission respectively.

Infections of the respiratory tract were noted in eleven of the patients and verified as relatively mild inflammations which are not accompanied by hyperpyrexia and febrile convulsions.

TABLE II. PROTHROMBIN LEVELS IN PATIENTS WITH SALICYLATE INTOXICATION

CASE	AGE	SALICYLATE LEVEL OF PLASMA (MG.%)	PROTHROMBIN LEVEL		HEMORRHAGIC MANIFESTATIONS
			PATIENT	CONTROL	
1	3 wk.	68.5	4'51"	1'5"	Petechiae Epistaxis Melena Xanthochromia of and crenated red cells in the spinal fluid
2	6 mo.	44.4	45"	55"	
3	26 mo.	40.0	2' 0"	1'15"	
4	8 mo.	65.2	1'45"	45"	
5	4½ mo.	42.3	40"	30"	Hemorrhage into both ventricles (post-mortem ventricular taps)
6	3½ mo.	41.6	70"	30"	
7	2½ yr.	18.2	35"	35"	
8	20 mo.	7.3	28"	31"	
9	5 mo.	20.8	1'55"	40"	Petechiae over chest and bloody emesis
		12 hr. later 13.3	2' 0"	30"	
		2 days later	50"	30"	
		3 days later	27"	30"	
11	21 mo.	15.9	38"	45"	
13	3½ yr.	7.3	10' 0"	1'40"	
		3 day 0.35	60"	50"	

Laboratory Findings.—The most outstanding laboratory findings concerned the changes in the acid-base equilibrium of the blood. The carbon-dioxide content of the serum of these patients before treatment was uniformly depressed with a consistent lowering of pH. The younger patients showed more profound changes in this shift to acidosis than the older ones. The next most consistent laboratory feature (Table II) was a prolongation of prothrombin time in six of the eleven patients. Clinical evidence of hemorrhage was noted in only two patients. Electroencephalograms were done on three patients; one showed abnormal tracings on the twelfth day of hospitalization. Three months later they were still abnormal; however, normal tracings were obtained nine months after

hospitalization.* Serum chlorides were usually normal or elevated; only two were slightly below normal. The majority of glucose determinations yielded normal values. The initial nonprotein nitrogen values were slightly elevated. In one instance (Case 5) there was evidence of renal failure with 118 mg. per cent nonprotein nitrogen, 8 mg. per cent calcium, and 7.5 mg. per cent inorganic phosphorus. This patient died, and no autopsy was obtained. Urinary findings included albuminuria, positive Rothera test and persistence of positive ferric chloride test on boiling, as well as many granular casts on microscopic examination. Cases 11, 12, and 13 (Table III) showed low urine pH values before treatment; succeeding values on the second and third days of hospitalization showed a rise in urinary pH. On the third day of hospitalization there was still a positive Rothera test as well as a persistent though decreasingly positive ferric chloride test on boiling of the sample.

TABLE III. URINARY FINDINGS IN PATIENTS WITH SALICYLATE INTOXICATION

CASE	DAY OF HOSPITALIZATION	SALICYLATE LEVEL IN PLASMA (MG.%)		URINE		
			$FeCl_3$	ROTHERA	pH	Chlorides Gm. NaCl/ L. Urine
10	1	38.8	++++	+++	--	--
	2	21.4	++++	++++	--	--
	4	3.2	++++	++	--	--
	5	----				
11	1	15.9	+++	+++	5.0	1.4
	2	----	+	+++	6.0	1.1
	3	0.6	trace	++	7.0	--
12	1	1.7	±	+++	4.5	3.4
	16 hr. after admission	1.3	±	+++	5.0	3.4
	2	0.2	-	+	7.0	--
13	1	7.3	++++	++++	5.19	--
	2	1.35	±	++++	5.0	--
	3	0.35	trace	++	7.0	--

The spinal fluid was examined in nine of the cases and showed a positive Rothera test as well as ferric chloride, even with boiling of the sample. In only one case (Case 1) were crenated red blood cells as well as xanthochromia noted.

Total ketones as acetone and base-binding ketones of the blood were determined in Case 10. The base-binding ketones amounted to 11 milliequivalents per liter. The significance of this is apparent when one observes that the bicarbonate value is depressed from normal value of 20 to 25 milliequivalents per liter to approximately 12 milliequivalents per liter.

Salicylate Determinations.—Plasma salicylate determinations showed at the time of entry, levels of 40 mg. per cent and higher in the younger patients who demonstrated the most severe type of intoxication. Lower concentrations were found more frequently in the patients older than 20 months. In almost all of these instances the initial pH of the serum was low normal or slightly below normal with corresponding carbon-dioxide content of the serum between 25 and 35 volumes per cent. The highest concentration of salicylate in

*This patient never has had epileptic manifestations, either before salicylism or up to June, 1946.

the plasma, 68.5 mg. per cent, was found in the 3-week-old infant who had received a total of 1.5 Gm. of aspirin in two days. Table IV shows the amount of salicylate administered to each patient insofar as it was possible to gain this information. For comparison, there are tabulated the dosages recommended by Marriott and Jeans[7] for infants. In most of these patients the doses administered were greater than that within the range of safety calculated by Marriott and Jeans. Some of these patients received dosages of salicyl compounds as great as those dosages recommended for therapy in acute rheumatic fever in older children[8] and for young adults.[9]

TABLE IV. COMPARISON OF ASPIRIN DOSAGES RECEIVED WITH THOSE RECOMMENDED AS SAFE

CASE	MAXIMUM RECOMMENDED* DOSE (GRAINS/DAY)	MAXIMUM DOSE RECEIVED (GRAINS/DAY)	DURATION OF MEDICATION (DAYS)	SALICYLATE LEVEL OF PLASMA (MG.%)
1	½	11¼	2	68.5
2	3	27	1	44.4
3	13	7½	2	40.0
4	4	8 pills daily (?)	4	65.2
5	2	17	3½	42.3
6	2	10-15 (mother vague)	1	41.6
7	15	22½	2	18.2
8	11	8 tsp. unknown medication	2½	7.3
9	2½	10-20	3	20.8
10	12	42	3	38.8
13	21	12	2	7.3

*On basis of amounts recommended by Marriott and Jeans—1 grain per year of age every four hours.

Therapy.—All of the patients except one received M/6 sodium r-lactate in Ringer's solution by the intravenous and subcutaneous routes immediately on admission to the hospital in amounts indicated in Table V as cubic centimeters of M/1 sodium r-lactate per kilogram of body weight. A five per cent glucose solution was given hypodermically and in most instances at several intervals by intravenous and subcutaneous routes until oral feeding could be resumed. Parenteral vitamin K and vitamin C were given to all patients. In addition to vitamin K, small whole blood transfusions were used to combat hemorrhagic tendencies.

The patients in severe acidosis were also in a state of circulatory collapse, and though their respirations were exaggerated, their skin was ashen gray. Oxygen was given to these patients, and they were bundled in warm blankets; however, the restoration of fluids and electrolytes did more to overcome the state of circulatory collapse.

Course.—The response to treatment varied in each of these patients, and all except two of them showed clinical improvement to some degree in one to two hours following treatment. One of these patients (Case 5) died; the other (Case 13) showed no improvement with glucose and M/40 lactate Ringer's solution for twenty-two hours; response was good after M/6 sodium lactate solution was given (Table V). Those who were treated for severe acidosis, who were in a state of circulatory collapse, and who had high levels of salicylate, were slow to overcome their lethargy even though they were no longer comatose. This is in contrast with the usual rapidity with which the

TABLE V. BLOOD CHEMISTRY STUDIES BEFORE AND AFTER TREATMENT

CASE	TIME	M/1 Na-r-Lactate c.c./Kg.*	MG.% SALICYLATE		SERUM pH	CO_2 CONTENT (SERUM VOL.%)	SERUM CHLORIDE (Mg.% NaCl)
			PLASMA	SPINAL FLUID			
1	1 P.M.	10	68.5	17.5	7.13	15.8	631
	4½ hr.	5	38.2		7.41	47.0	
	21 hr.		35.6	9.4	7.41	50.4	
	II day		20.9		7.47	58.5	
	III day		8.0		7.55	64.5	
	IV day		trace		7.58	74.8	
2	12 P.M.	15	44.4	15.7	7.20	16.7	680
	9 hr.		33.6		7.51	51.6	
	II day		1.5		7.49	60.5	
	V day		trace				
3	11 A.M.	9	40.0	11.8	7.33	25.8	
	5 hr.		35.4		7.50	43.5	
	22 hr.		23.1		7.51	50.8	
4	1 P.M.	15	65.2	26.0	7.20	20.4	
	7½ hr.				7.46	36.7	
	20 hr.		42.6		7.47	63.0	
5	9 A.M.	5	42.3	14.6	7.27	16.0	703
	1 hr.				7.30	29.0	
	2½ hr.				7.43	35.0	
	4½ hr.				7.52	36.0	
	7 hr.				7.48	47.0	
6	6 P.M.	11	41.6	8.0	7.16	14.0	679
	16 hr.				7.32	51.0	
	23 hr.		29.5				
	II day		9.7				
	III day		3.2				
	IV day		0.8				
7	9 P.M.	9.2	18.2	3.2	7.30	26.0	580
	13 hr.		13.2		7.50	59.8	
	II day		trace				
8	on admission	5	7.3	1.04	7.32	31.0	
9	12:10 A.M.	5	20.8	6.25	7.32	38.0	560
	12 hr.		13.3		7.50	57.8	512
	24 hr.					66.0	568
10	3:30 P.M.	8	38.8	17.0		26.5	590
	4½ hr.				7.38	49.4	
	17½ hr.		30.6		7.43	45.6	
	23½ hr.		----		---	---	
	41½ hr.		21.4				
	58 hr.				7.46	60.6	
	65 hr.		11.8				
	89½ hr.		3.2			73.0	
	113½ hr.					76.3	
11	5 P.M.	10	15.9		7.31	20.0	594
	16 hr.		2.3		7.38		580
	23 hr.					55.5	
	48 hr.		0.6		7.43	60.0	572
12	5 P.M.	5	1.7		7.31	34.0	570
	16 hr.		1.3		7.44	51.5	571
	40 hr.		0.2		7.45	62.0	604
13	2 P.M.		7.3		7.32	37.0	540
	21½ hr.	10	1.33		7.35	36.0	552
	45½ hr.		0.35		7.44	56.0	570

*Sodium-r-lactate diluted to M/6 in Ringer's solution. Patients also received glucose parenterally.

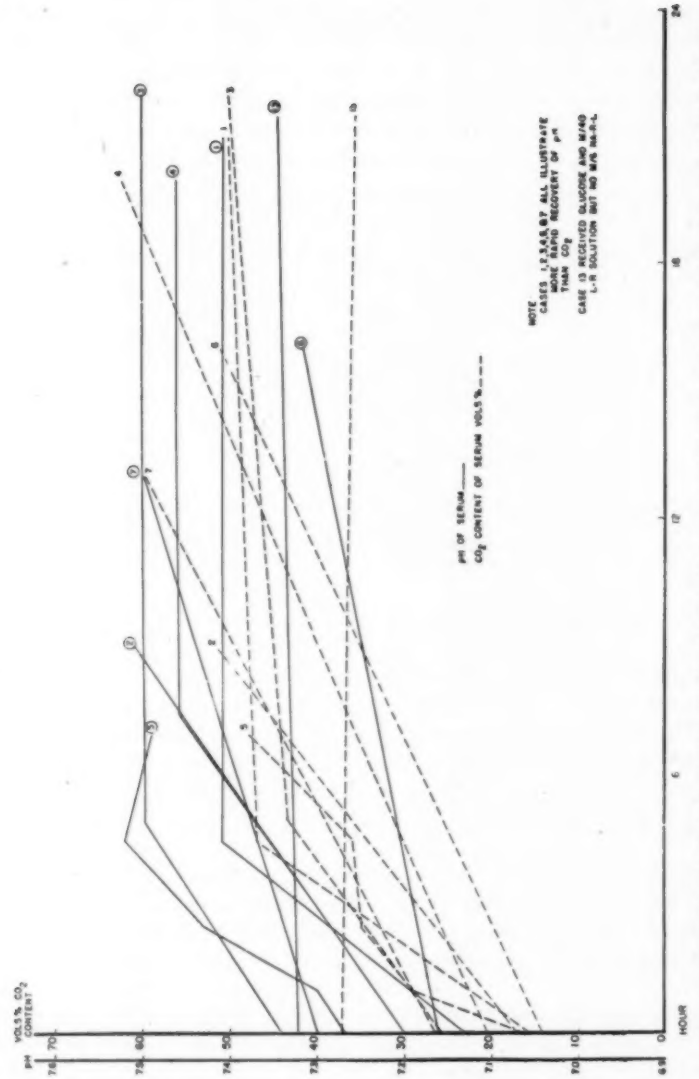
VOL.% CO2 CONTENT
pH
HOUR
pH OF SERUM
CO2 CONTENT OF SERUM VOL.%
NOTE
CASES 1,2,3,4,5,6,7 ALL ILLUSTRATE MORE RAPID RECOVERY OF pH THAN CO2
CASE 13 RECEIVED GLUCOSE AND M/40 L-R SOLUTION BUT NO M/6 NA-R-L

Fig. 1.—Illustration pH and carbon dioxide before and after treatment of metabolic acidosis from salicylate intoxication (Cases 1 to 7, and Case 13).
(Case 13. This patient was given M/6 sodium r-lactate immediately following the last determination of serum pH and carbon dioxide represented in this figure.)

diabetic who has just recovered from acidosis quickly overcomes his lethargy. In Fig. 1, showing the individual recoveries of the patients, and in Table V it is shown that the pH of the serum returned to the range of normal before the carbon-dioxide content (principally bicarbonate) of the serum was restored to the range of normal. A similar pattern of restoration of acid-base balance has been observed in diabetics[10] whose recovery from acidosis has been studied by the method of Shock and Hastings.[11] The cause here would seem to be continued hyperpnea on the basis of salicylate in spite of relief of acidosis.

Rapid recovery (Table V and Fig. 1) of acid-base equilibrium was uniform except in the two instances (Cases 5 and 13) mentioned. Cases 1, 3, and 10, within five hours after treatment, showed restoration of the pH and carbon-dioxide content of the serum to normal. In contrast to the rapid recovery of acid-base equilibrium, the salicylate disappeared slowly from the blood, and appreciable amounts were found on the second and third days of hospitalization as can be seen in Table V.

Mortality.—All but one of these patients showed an ultimately good clinical response to therapy given. This was the patient (Case 5) who had elevated non-protein nitrogen of 118 mg. per cent. He was 4½ months old and expired eleven hours after admission. At the time the last laboratory determinations were available, the patient's acid-base equilibrium was found to be within normal range; serum pH was 7.48, and the carbon-dioxide content had risen to 47 volumes per cent. Although this restoration of acid-base equilibrium proceeded gradually, as can be seen from Table V, there was no coincident improvement in the clinical condition of the patient. The initial sample of spinal fluid gave no signs of hemorrhage; however, post-mortem intraventricular taps showed bloody fluid despite administration of vitamin K. No necropsy data are available.

EXPERIMENTAL STUDIES

Several older children were given salicylate experimentally as aspirin or sodium salicylate for three to six consecutive days. These children were from 5 to 12 years of age, and as a group demonstrated different effects of salicylate on respiration, pH, and carbon-dioxide content of the serum. The results are given in Table V. Case E1 exhibited severe hyperventilation on the third day; however, the serum pH was at the upper limits of normal and the carbon-dioxide content slightly depressed. Case E5 had only slight hyperpnea, but developed severe anorexia and vomiting with marked lowering of pH and carbon-dioxide content as can be seen in Table VI. Case E7 showed no effect at all, even on the sixth day when the concentration of salicylate was 35.8 mg. per cent in her plasma. She was the oldest of these four patients. It should be emphasized that all of these patients had good caloric and liquid intake prior to and during administration of salicylate, and only as mentioned in Case E5 was there severe anorexia and vomiting.

The absorption of aspirin and sodium salicylate following single and multiple oral doses was studied in a group of children. From the absorption curves of both sodium salicylate and aspirin on patients with varying single doses (see Figs. 2 and 3) it appeared that there would be an accumulation of

the salicyl compound when given at the usually advised interval of every four hours. These compounds when so given for several days did show an increase in the level from day to day (Fig. 4). The actual accumulation was tested on a single subject and compared with the hypothetical effect. This was done by giving a single dose (.043 Gm. per kilogram) of sodium salicylate by mouth and observing the gradual rise and fall of the plasma salicylate level. The rate of absorption was slow because enteric coated tablets were used. Following this procedure a second test was performed by giving the same dose of sodium salicylate every four hours. At the end of twenty-four hours the experiment was terminated because the subject experienced tinnitus nad nausea and began to vomit. The actual values obtained during the second test are plotted in Fig. 5 on the broken line curve and do not deviate much from the hypothetical curve showing accumulation by superimposition of the single dose absorption curve at four-hour intervals.

TABLE VI. VARIOUS REACTIONS TO SALICYLATE AS SEEN IN OLDER CHILDREN GIVEN THE DRUG EXPERIMENTALLY

CASE	AGE	DOSE (GM./KG./24 HR.)	DURATION (DAYS)	MAXIMUM SALICYLATE LEVEL OF PLASMA (MG.%)	pH	CO_2 (VOL.%)	HYPERVENTILATION	ACID-BASE REACTION
E1	10	.17 Na salicylate	3	48.5	7.45	40.4	severe	early respiratory alkalosis
E5	6	.19 Na salicylate	6	54.2	7.25	23.8	slight	metabolic acidosis
E6	5	.30 Na salicylate	4	55.4	7.31	24.4	moderate	metabolic acidosis
E7	12	.12 aspirin	6	35.8	7.41	45.6	none	normal

DISCUSSION

In order that an infant or young child not be allowed to become seriously intoxicated with salicylates, it would be well for physicians and especially pediatricians to educate and warn parents of these potential properties of aspirin and other salicylate compounds. This is done and wisely so in the case of the sulfonamide compounds. Why is it not done with salicylate compounds?

Certainly the use of salicylate compounds for purposes other than symptomatic relief is not justified. Infection should be combated by specific measures. Almost all drugs have untoward effects, and these are proportionately intensified with larger doses. In therapeutics, these harmful effects must not outweigh the beneficial effects if drugs are to be used advantageously. Even with supervision in administration of salicylates in older and larger children who are capable of making known their complaints, the medication can produce serious and sometimes fatal intoxication.[12]

Stevens and Kaplan[12] found that children of ages 9 to 11 did not tolerate the massive doses of salicylate which achieved blood plasma levels considered by Coburn[8] to be therapeutically beneficial yet unharmful in adults. They also observed that it was not easy to maintain the concentration of salicylate and that it was necessary to manipulate the dosage from day to day and de-

termine the actual concentration in the plasma. Furthermore, they stated that the drug accumulated, and it was because of this that they found it necessary to alter the dosage. The efficacy of this massive dosage is questioned by Wégria and Smull.[13] Fashena and Walker[14] also demonstrated that the dosages could be decreased by 30 to 35 per cent of the initial twenty-four hour dose without significantly altering the concentration of salicylate in the blood plasma. Guest and associates[15] found that the effect of salicylate appeared to be proportional to the dose administered, and also noted that this effect increased with the duration of medication. We have shown that there may be an accumulation of salicylates in the blood from day to day.

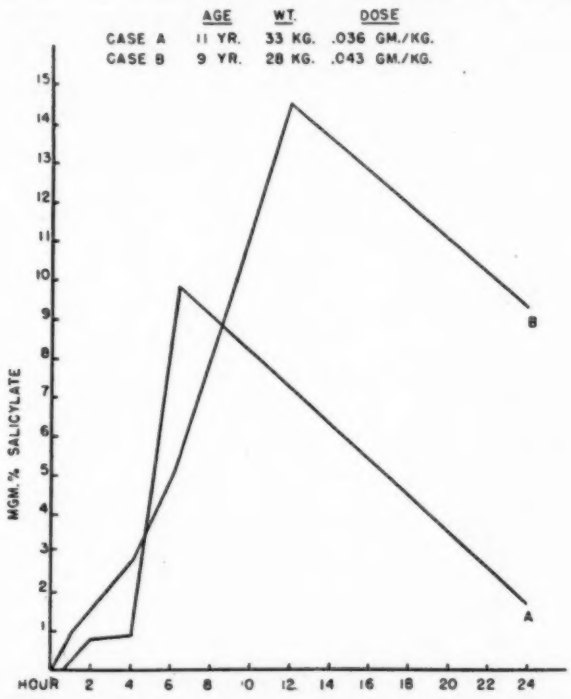

Fig. 2.—Rate of absorption of oral sodium salicylate (single dose). Salicylate values apply to plasma concentrations.

Because of the serious and progressive nature of salicylate intoxication, the evident necessity for an early diagnosis, especially in infants, cannot be overemphasized. By far the most common symptoms of poisoning in this very young group of patients were hyperpnea, fever, listlessness, and even coma, pallor, and cyanosis. With the listlessness came disinterest in feeding procedures. Less prominent were dehydration, which was slight to moderate, vomiting, and convulsions. Two patients presented clinical evidence of hemorrhagic phenomena, and in another patient hemorrhage into the ventricles was found on post-mortem intraventricular puncture.

In the absence of renal failure, diarrhea, diabetes, and other severe infections, the combination of hyperpnea, listlessness, and fever should suggest salicylate intoxication as a likely diagnosis. A more direct approach to the problem of an early diagnosis can be achieved by obtaining a careful history of medications given to the patient. Since fever is such a prominent finding, as noted by Dodd and associates[16] and Barnett and associates,[1] the error of giving salicylates as supportive treatment to alleviate hyperpyrexia can best be avoided by ascertaining the diagnosis first. It is entirely possible that many of our cases of intoxication resulted from prolonged use of aspirin for fever which in reality became a toxic

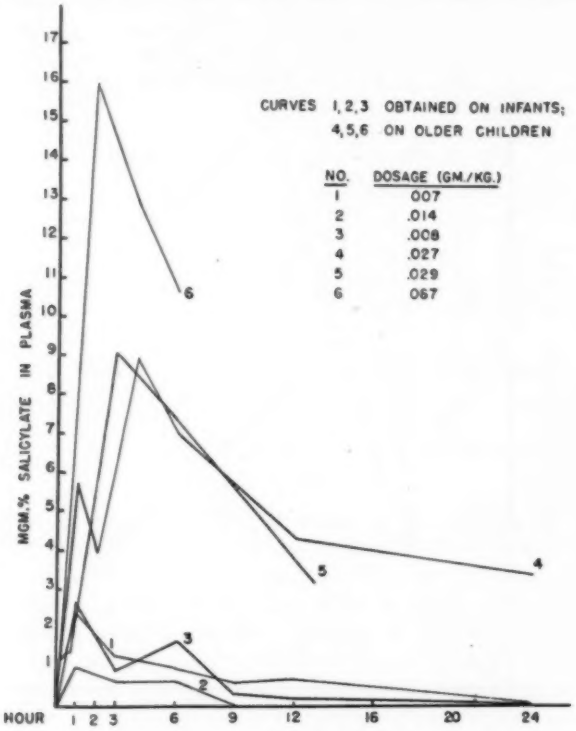

Fig. 3.—Rate of absorption of aspirin (single oral dose).

manifestation of aspirin. This clinical picture together with the laboratory findings of distorted acid-base balance and positive urine ferric chloride test on boiling confirms the diagnosis. A determination of plasma salicylate will complete the picture. Other procedures may reveal other toxic effects from salicylate, such as prolonged prothrombin time,[17-19] hypocoagulability of the blood,[20] epistaxis,[21] hemorrhages into the stomach[22, 23] and brain,[24] granulocytopenia,[25] toxic hepatitis,[26] low vitamin C content as found in animal tissues by Ritz and associates,[27] or increased vitamin C output into the urine,[28] and even lowered renal clearance[29] and evidence of renal damage which may be temporary.[30]

The general condition of most of these young patients gives indication of the need for prompt treatment. Therapy includes treatment of acidosis by administration of M/6 sodium r-lactate in Ringer's solution and glucose parenterally; relief of dehydration and ketosis is also achieved by this procedure. Case 13 clearly illustrated the response of a patient in acidosis when treated with glucose and M/40 lactate Ringer's solution instead of M/6 sodium r-lactate in Ringer's. The carbon-dioxide content of the serum and pH of the urine remained abnormally low for twenty-two hours, and they did not respond until a full dose of M/6 r-lactate was given. (Tables III and V.) Dodd and associates[16] considered alkali useful for treatment late in the course of intoxication when acidosis developed. Rapoport and associates,[31] in testing the effect of sodium bicarbonate on salicylate intoxication in dogs, observed that the

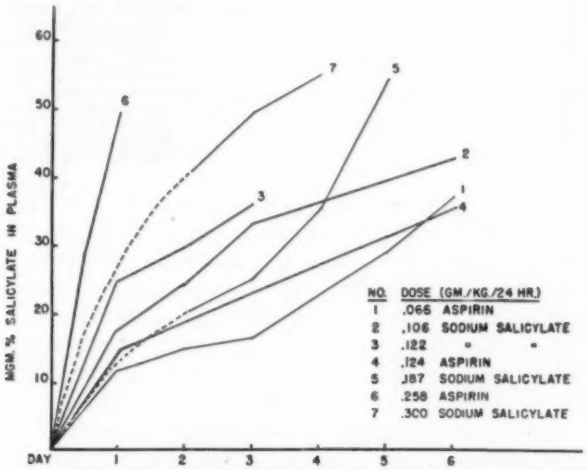

Fig. 4.—Plasma concentration of salicylate with oral aspirin and oral sodium salicylate (divided doses at four-hour intervals).

duration of the intoxication was shortened in spite of an already existing tendency for respiratory alkalosis. One of their animals did develop fatal tetany. Vitamin K and small, whole blood transfusions are indicated on the basis of the ever increasing evidence of hemorrhagic phenomena reported in the literature,[14, 32] and our own findings. Without studies prior to the onset of salicylate intoxication, it is not possible to evaluate the need for vitamin C; however, the work of Ritz and associates[27] and Daniels and Emerson[28] and the usual history of the patient serve to provide rationale for parenteral and later enteral vitamin C. Undue exposure of these patients should be avoided in spite of hyperpyrexia. The use of cool oxygen is not contraindicated and appears to be stimulating. Whenever there has been a history of recent ingestion of a large amount of aspirin or other salicylate compound, gastric lavage is a very important procedure and should not be omitted.

Serum pH and carbon-dioxide determinations can be repeated at four- to six-hour intervals following treatment if the patient seems to be doing well

clinically. These should be done more frequently if indicated, and additional lactate may be necessary if the patient is severely acidotic, although the majority of our patients did not need additional M/6 sodium lactate solution. Early in the course of treatment, color, responsiveness, and activity are better criteria of clinical status than respirations. The reason for this is that with the administration of fluids the patient seems to obtain a "second wind" and can improve respiratory efforts in attempting to blow off excess carbonic acid. Therefore, with the improvement in the general condition of the patient, he responds to the physiologic demand for increased respiration. Following the

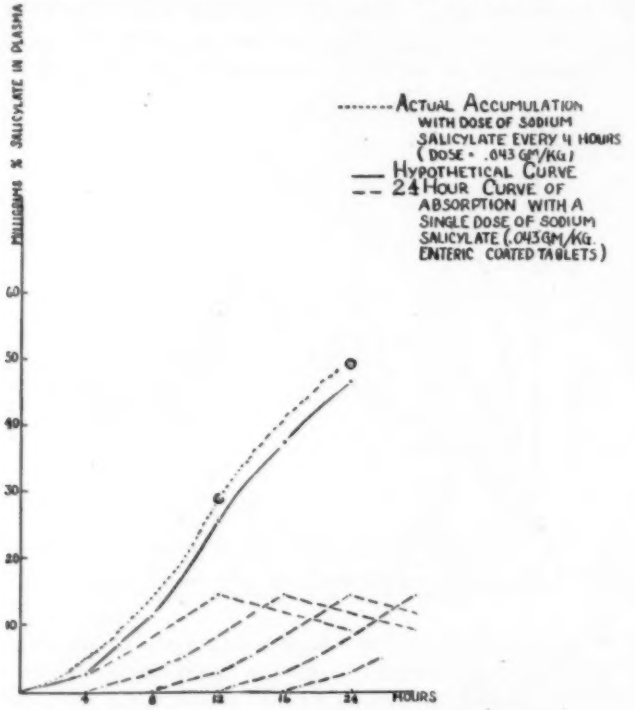

Fig. 5.—Cumulative effect of salicylate.

establishment of the proper ratio of sodium bicarbonate and carbonic acid concentrations and relief of ketosis, if there be sufficient concentration of salicylate, hyperventilation will continue because of the apparent, direct, stimulating effect of the salicylate.

The toxic manifestations due to salicylates are manifold, and, moreover, the incidence of a given symptom appears to vary in the different age groups. For example, we have named the most common symptoms associated with severe and acute intoxication in infants which, of course, do not include such complaints as vertigo, tinnitus, headache, and deafness. These are correlated with the ability of self-expression. Other reactions described in the literature

and not yet mentioned include urticaria, anaphylactic reaction, and gastrointestinal irritation which may be associated with gastric ulceration and toxic encephalopathy. Coburn states that there was no evidence of prolonged prothrombin time in his patients who were adults.[9] There is evidence from the literature[14] as well as from our own data (Table II) that this occurs in children and infants.

The literature has become confused, particularly with reports which would seem to be conflicting because one or another form of acid-base imbalance is emphasized. A part of this confusion may arise because the determination of carbon-dioxide content of the serum is not supplemented by a pH determination of the serum and urine; part of it may also arise because an attempt is made to compare results on anorexic younger children and infants with experimental results obtained on older children, adults, and even animals, whose usual caloric and liquid intakes have not been affected prior to or during the period of study. These results cannot be applied interchangeably. Ketosis, for example, occurs with greater rapidity in children than in adults. Emphasis should rather stress the different kind and degree of salicylate intoxication that is developed in individuals, as we have shown in our experimental group (Table VI).

The evidence of a respiratory type of alkalosis similar to that developing in the first case of the experimental group (E1, Table VI) has been seen also in the older individuals on which it is presumed that Odin[34] bases his conclusions, since he does not designate the age group that received such large doses of salicylate. Coburn,[9] however, found no such effect. A shift of acid-base balance to respiratory alkalosis was observed by Ryder[35] in one case of a 16-year-old Negro patient, and by Guest and associates[15] in children 3 years of age and over. In dogs, Dodd and associates[16] found only a slightly elevated pH in a phase of panting. Dodd, however, did not find too great a similarity in the pattern of intoxication in dogs and infants. In experiments on monkeys and dogs, Rapoport and associates[31] found primary hyperventilation with lowering of carbon-dioxide tension in blood with or without decrease in bicarbonate. They also observed that pentobarbital sodium could suppress hyperventilation and restore pH and carbon dioxide to normal values. Morphine exerted a convulsant action without noticeable decrease of hyperpnea. The general condition of the dogs in the experiments of Dodd and associates[16] was remarkably good; the dogs ate eagerly and drank unusually large amounts of water throughout the entire experiment. This reaction is so strikingly different when contrasted with the pattern of reaction exhibited in young children and infants and is of such significance, that it must be emphasized. By the same token, reactions and tolerance exhibited by the adults preclude a fair transference or application of data obtained on such a group with that obtained in a group of young children or infants. Decreased intake of food, liquids as well as nutritious substances, is a key factor in the production of metabolic acidosis in infants. Sable[30] proposed that the ketonuria and ketonemia may be due to starvation from anorexia and vomiting or the toxic effect on cellular metabolism. Lutwak-Mann[36] found that respiration of rat liver and kidney

slices is inhibited by M/10 concentration of salicylates, and that liver glycogen disappeared almost completely four to six hours after salicylate injection. Similar work has not been done on human tissues.

To conclude the discussion of this difference in toxic effect of salicylate which exhibits one pattern of acid-base imbalance in a group of infants and a more variable pattern in the experimental group of older children, it may be said that there is a cycle which can be interrupted or aggravated at any phase. To understand the pattern of a given patient, many determinations can be done, but the most significant data are obtained from values of urine pH, blood pH and carbon dioxide. The cycle, from all available information, is one of hyperventilation caused by salicylate, uncompensated respiratory alkalosis, then compensation rapidly brought about by the kidney with excretion of excess bicarbonate. Ketosis, which may be present even before administration of salicylate, but is certainly aggravated by it, produces a shift toward metabolic acidosis. Since hyperventilation caused by salicylate (either by central or reflex stimulation) is already in operation, it soon begins to fail because of muscular fatigue and lethargy which are early and prominent factors in the infant. The onset of metabolic bankruptcy on the basis of starvation and increased metabolism takes its toll more quickly in the infant. With the depletion of sodium bicarbonate enhanced by ketosis, it becomes even more imperative for hyperventilation to continue, so that there will not be a relative excess of carbonic acid. At this point, when hyperventilation has become a physiologic necessity and not merely a manifestation of salicylism, the respiratory center may have undergone poisoning, or the patient may lag because of the inability to keep apace with all that has transpired. If either of these factors operates (and it can be readily understood that the infantile tissues cannot cope as long with such odds as the adult), then metabolic acidosis ensues. On the average, respiratory efforts seem only 50 per cent efficient. In the early phase of the cycle, urinary pH is alkaline, coinciding with excretion of sodium bicarbonate; however, later, the pH reverts to acid values coinciding with the phase of metabolic acidosis.

CONCLUSIONS

1. Thirteen cases of salicylate intoxication in infants and very young children are discussed.

2. The most severe type of reaction occurring in this group is a disturbance of the acid-base equilibrium. Other types of reactions were encountered less constantly.

3. At the time of hospitalization, all patients showed a metabolic acidosis with a lowered pH and carbon-dioxide content of the serum.

4. Salicylates, given experimentally to older children whose usual caloric and liquid intake were maintained, produced less regular, if any, signs and symptoms of toxicity.

5. Salicyl compounds, when given in dosages from 0.066 Gm. per kilogram per twenty-four hours in six divided doses (approximately ½ grain per pound),

tend to accumulate in significant amounts in the body, as shown by determinations of plasma levels.

6. In view of the dangers and possibility of fatality in infants, it is suggested that aspirin be given not at all or very cautiously, with full awareness of all its properties for intoxication. These same possibilities for intoxication in one form or another obtain in older individuals, but to a lesser degree.

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TUBERCULOUS DACTYLITIS IN CHILDHOOD: A PROGNOSIS

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BALTIMORE, MD.

THE spontaneous healing of remarkably destructive tuberculous lesions of the small bones of the hands and feet (metacarpals, metatarsals, and phalanges) observed over the past decades in the Harriet Lane Home has led to the present study of cases recorded in the diagnostic index of the clinic. Twenty-one cases were selected for analysis because of adequate clinical and laboratory examination and follow-up.

Each patient reacted positively to intradermal, tuberculin skin testing and had a negative blood Wassermann test. All but three showed roentgen-ray evidence characteristic of pulmonary or mediastinal tuberculosis. All patients were below the age of 14 years when first examined in the Harriet Lane Home. Nine of the twenty-one patients gave a history of exposure to sputum-positive tuberculosis.

Incidence.—In the special tuberculosis clinic where 610 children infected with tuberculosis under 2 years of age have been registered since 1928, tuberculous dactylitis has been recognized in only four patients, giving an incidence of 0.6 per cent. In addition, since only forty-three cases in all have been recorded during the past three decades at the Harriet Lane Home where the incidence of tuberculosis is quite high, it is apparent that tuberculous dactylitis is a relatively rare complication. This is in rather marked contrast to the figures of Herzfeld and Tod[1] (6 per cent) and of Benci and Mezzari[2] (4.21 per cent).

From a clinical viewpoint the patients fall into two groups: Group I consists of eleven individuals who had tuberculous dactylitis as a minor manifestation of a severe generalized infection;† Group II includes ten patients who had a relatively mild tuberculous infection and whose dactylitis, the presenting symptom in eight instances, was one of the minor complications.‡

Color, Age, and Sex.—There is no significant difference between the two groups with respect to color, age, and sex. It is of interest, however, that sixteen (76 per cent) of the total number of patients were negro. It is significant that fourteen (67 per cent) were under 2 years of age at the time when this complication was observed. This conforms with Dr. Brailey's[3] findings demonstrating that tuberculosis is a more severe disease in infancy than in later childhood.

Length of Follow-up.—The average length of life after recognition of the disease of the patients in Group I (with the exceptions noted above) was two and one-half years, with a minimum of seven days and a maximum of five years.

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*Fourth year medical student.

†All but three of these patients subsequently died of tuberculosis. Two of these may be presumed to have died because of the presence of very extensive lesions when last seen. The third patient is still alive after twelve years, but has numerous, active, tuberculous lesions.

‡The tuberculous lesions of these patients healed completely and, with one exception, left no residual disability or deformity, as the accompanying x-rays show. With the exception of one child who died of pyogenic meningitis, all of these individuals are living and well, and at present show no evidence of active tuberculosis.

The follow-up of the children in Group II averaged eleven years, with a minimum period of one and one-half years and a maximum of twenty-eight years.

Primary Tuberculous Lesions.—As a whole, children in Group I appeared more ill and had more extensive tuberculous lesions than those in Group II. As Table I shows, in Group I eight of the eleven patients had severe pulmonary lesions; the remaining three showed marked enlargement of the mediastinal nodes. However, in Group II only two of the ten patients had parenchymal lesions, five had enlarged mediastinal nodes, while three had only slight, nonspecific infiltration at the lung roots.

TABLE I. FINDINGS ON ROENTGEN-RAY EXAMINATION OF CHEST OF TWENTY-ONE CHILDREN WITH TUBERCULOUS DACTYLITIS

GROUP	TOTAL NO.	PARENCHYMAL PULMONARY TUBERCULOSIS	MEDIASTINAL TUBERCULOSIS	NONSPECIFIC ROOT INFILTRATION
Group I	11	8	3	0
Group II	10	2	5	3

Clinical Picture.—The local clinical picture was essentially the same in both groups of patients. The infected phalanx presented a fusiform, indurated swelling, usually painless. Fluctuation was present if the tuberculous lesion had broken through the periosteum of the bone with resultant abscess formation. The overlying skin was usually taut, shiny, and red. In only one instance was there a preceding history of trauma. Fistulas formed in eight lesions. Where the metacarpal or metatarsal bones were involved, the swelling appeared mainly on the dorsal surface, the area where the three fistulas recorded also appeared. Quite significantly, the "painless swelling" of the fingers was the presenting complaint in eight of the ten patients in Group II and of three in Group I, while other symptoms of a tuberculous infection were the chief complaint in the remaining eight. The average duration of the dactylitis before examination was two months in Group I and four months in Group II. However, the dactylitis was either the presenting complaint or an early sign in nineteen of the twenty-one children studied.

Other Types of Tuberculous Complications.—All eleven patients of Group I had other complications of the primary tuberculous infection, the most common, apart from serious involvement of the lung parenchyma in eight instances, being infections of other bones (radius and ulna three, tibia three, mandible three, spine two, orbit one, humerus one, and sternum one), cervical adenitis six, skin tuberculids two, and peritonitis one. The predominant tuberculous infection was bone and joint tuberculosis (eight patients) and miliary tuberculosis (three patients). However, five, or one-half of the children in Group II, had no evident complications other than dactylitis. Of the remaining five, involvement of other bones (radius and ulna two, spine one, and tibia one), biliateral phlyctenular keratitis one, cervical adenitis one, and peritonitis one, constitute the known complications.

X-ray Findings.—(See Figs. 1 to 14.) From the accompanying photographs of x-ray plates and films, one may see that the tuberculous lesions of the small bones assume many varied forms, from minimal medullary changes and periosteal

Fig. 1.—L. B., aged 2 years, with severe pulmonary tuberculosis and multiple metastatic tuberculous bone lesions. Destructive lesions are seen in ten of the small bones of the hands; soft tissue swelling is seen in the neighborhood of the more severely involved bones.

Fig. 2.—L. B., aged 5½ years, showing good partial healing of the lesions in the right hand but progression of the lesion in proximal phalanx of the index finger, left hand.

reduplication, said to distinguish tuberculosis of the phalanges, metacarpals, and metatarsals from tuberculous infections of other bones,[4] to "ballooning" of the cortex and widespread destruction of all layers of the bone. It will be seen that the primary and most extensive lesion is usually localized in the diaphysis. From the follow-up films on the patients in Group II it is seen that the normal structure of the bone is usually completely restored, and, from examination at this time, that no disability in function has resulted. In one exception, the lesion was inadequately treated during its active phase and a subluxation of the second phalanx at this time was allowed to heal uncorrected.

Fig. 3.—L. B., aged 16 years. The bones of the right hand have returned almost completely to normal; there is marked shortening of the proximal phalanx of the left hand, with resultant deformity.

Sites of Lesions.—Among all of the children studied, the number of bones involved in both hands and feet totaled fifty-four, twenty-eight in Group I and twenty-six in Group II. The bones of the hands were much more frequently affected than those of the feet, forty-eight in the former and six in the latter. Of the lesions in the hands, twenty-six (55 per cent) were localized in the proximal phalanx, sixteen in the metacarpals, and six in the second phalanx. No lesions were seen in the terminal phalanx of any finger or toe. The most common sites were the proximal phalanx of the index and middle fingers and metacarpals of the middle and ring fingers of the hands. There was no significant difference between the two hands, twenty-three bones of the right hand and twenty-five of the left hand being involved. Among the small bones of the feet, the proximal phalanx of toes 1, 3, and 4 were each involved once, and the

Fig. 4.—L. B., aged 2 years. Feet show destructive tuberculous lesions of first phalanx of right great toe and of the first and fifth metatarsals on the left. Note swelling of soft tissue of left foot.

Fig. 5.—L. B., aged 16 years. Feet: complete healing and restoration to normal contour has occurred in the lesions present fourteen years before, in the first phalanx, right great toe, and the fifth metacarpal left. Healing of the severe lesion, formerly present in the first metacarpal left, has been accompanied by considerable shortening of the bone and resultant deformity.

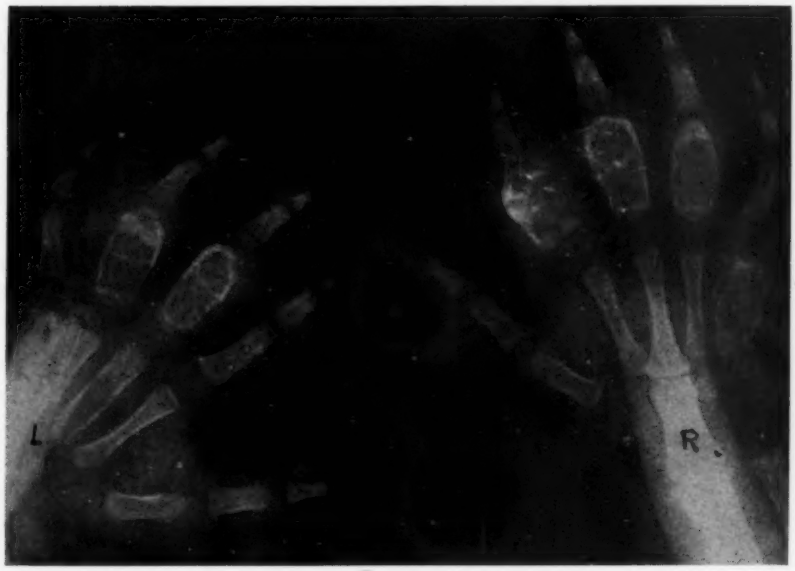

Fig. 6.—M. Y., aged 2 years. Chest film showed nonspecific root infiltration, tuberculin test positive. Destructive lesions in fifth metacarpal right, in the proximal phalanx of the second, third, and fourth digits on the right, and the third and fourth digits on the left, with marked soft tissue swelling.

Fig. 7.—M. Y., aged 23 years. The bones of the hand have returned completely to normal.

Fig. 8.—M. Y., aged 2 years. Tuberculous involvement of first metatarsal, right.

Fig. 9.—M. Y., aged 18 years. Bones of feet are now entirely normal.

Fig. 10.—M. T., aged 2 years. Mediastinal tuberculosis with phlyctenular keratitis and tuberculous lesions of the first and third metacarpals and proximal phalanx of third finger on left hand and of the proximal phalanx of the fourth finger right hand. Note periosteal reduplication.

Fig. 11.—M. T., aged 2 years. There are severely destructive lesions in the proximal phalanx of the fourth digit right hand and third digit left hand. The lesions previously seen in the metacarpals are much improved.

first metatarsal on three occasions, with a total of six lesions. Multiple lesions of the hands and feet occurred in seven patients of Group I, and five of Group II. One patient in the first group (Figs. 1 to 5) has lesions in the proximal phalanx of fingers 1, 2, 3, and 5 of his right hand, middle phalanx of finger 5 of this hand, proximal phalanx of fingers 1, 2, and 3 of his left hand, of metacarpal 4 of this hand, and of metatarsal 1 and the proximal phalanx of toe 1 of his left foot. These healed with minimal shortening of two bones (Fig. 5).

Fig. 12.—M. T., aged 8 years. The bones of the hands are normal except for slight thickening of the proximal phalanx of the right fourth and left third digits.

Prognosis.—With the exception of patient L. B., who is alive at present, and two patients who are presumed dead, all patients in Group I died of their tuberculous infection. In Group II all of the patients are living and in good health except for one already mentioned. Adequate serial x-rays are not available for definite statements as to time taken for healing of the dactylitis, but on the basis of three cases, mild lesions had completely disappeared within thirteen months, moderately severe ones within two years, and extensive destructive lesions within a minimum period of three years. From the histories of the patients, the lesions were found to be usually asymptomatic within eighteen to thirty-six months, provided the patients had a favorable prognosis as far as the rest of their infection was concerned and that they received adequate orthopedic care. The treatment consisted of immobilization of the affected digits in splints or casts for the period during which the lesion was active, and incision and drainage where the lesion was secondarily infected. In view of the strik-

Fig. 13.—M. T., aged 2½ years. Destructive lesions in the proximal phalanges of the first and fifth toes of the right foot.

Fig. 14.—M. T., aged 5½ years. The bones of the feet have now almost returned to normal.

ing x-ray findings, it would appear that amputation or dactylectomy is definitely contraindicated. Of the four patients whose digits were amputated (and who were not included in this series), no change in the prognosis of their general condition was found; all had minimal tuberculosis.

DISCUSSION

Tuberculous lesions of the small bones occur with relative rarity, but this series followed in the Harriet Lane Home seems worthy of report because where the patient has survived the other manifestations of his tuberculous infection the return to normal contour and function of the diseased bones has been remarkably good.

SUMMARY

1. Twenty-one patients with tuberculous dactylitis complicating primary tuberculous infections in childhood were followed until death or to date (an average of eleven years).

2. Fourteen, or two-thirds of the patients, were 2 years of age or less when this complication occurred. Sixteen were negro and five were white. Eleven had dactylitis as a minor complication of a severe generalized tuberculosis, ten had dactylitis as part of a relatively mild infection.

3. The dactylitis was the presenting complaint in eleven patients.

4. The bones of the hands were involved eight times more frequently than those of the feet. The proximal phalanx of the index and middle fingers were the bones most frequently involved.

5. Provided the patient survived the other manifestations of tuberculosis, the prognosis for complete healing of the bone with return to normal contour in most instances was excellent. Healing occurred in from one to three years.

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ACUTE GLOMERULONEPHRITIS

A Review of Ninety Cases

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THIS report is an analysis of a series of ninety consecutive cases of children with acute glomerulonephritis at the Children's Hospital during the past three years (1943 through 1945). There were thirty-four white and fifty-six Negro patients; forty-six were male and forty-four were female. It is to be noted that there was only a slight preponderance in the number of male patients with acute glomerulonephritis in our series in contrast to the several large series reported by other authors[1] who found a rather noticeable predilection for males. Lyttle[2] in his report on 125 cases of acute nephritis in children observed a ratio nearly 2:1 for males. The average age of the ninety patients was 5.7 years; the majority were between the ages of 2 and 10 years and the youngest was 4 months of age (Table I).

Table I. Age, Race, and Sex Distribution in Ninety Patients With Acute Glomerulonephritis

	No. Patients	Per Cent
Age		
0-1 yr.	2	2.3
1-5 yr.	36	40.0
5-12 yr.	52	57.7
Race		
Negro	56	62.3
White	34	37.7
Sex		
Male	46	51.1
Female	44	48.9

Onset of Clinical Manifestations

The onset of symptoms began either simultaneously with or shortly after an acute febrile disease in 86 per cent of the children in this series. A history of preceding illness was not obtained in seven cases. A hiatus of seven to fourteen days after the subsidence of the symptoms of the primary infection was most common, but several patients were admitted with an accompanying infection of the respiratory tract or skin.

The most common predisposing infections were those of the upper respiratory tract, including nasopharyngitis, tonsillitis, and otitis media; a history of such an infection was obtained for 65.3 per cent of the patients. It has been reported[3] that a "deep" hemolytic streptococcal infection precedes the onset of acute nephritis in about two-thirds of the patients. In our series the severity of

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the preceding upper respiratory infection appeared to be of no particular significance since many of the precipitating infections were quite mild (Table II).

Skin diseases such as secondarily infected burns, impetigo, and infected eczema form the next largest group of preceding infections (10.2 per cent). Futcher[4] has recently reviewed the role of skin infections in the etiology of acute glomerulonephritis and reported the incidence to vary from 0 to 28 per cent. Scarlet fever was the cause in three patients (3.3 per cent) but may be a more common predisposing infection than this figure would indicate, for the contagion service of Children's Hospital is rather small and most persons with scarlet fever are referred elsewhere. The remaining group had a history of some other infection including pneumonia, sinusitis, mumps, cervical adenitis, and others. In three cases, two of which fall outside of the time limit of this series, acute nephritis occurred with congenital syphilis. All three patients were under 1 year of age. It is problematical whether this association between congenital syphilis and acute nephritis represents a primary invasion of the kidney by *Treponema pallidum* or a secondary involvement of the kidney resulting from the upper respiratory infection frequently found to coexist with congenital syphilis. In this regard, it is well to point out that congenital syphilis is the most common precursor of acute glomerulonephritis in infants under 1 year of age.[5]

TABLE II. PRECEDING INFECTIONS IN THE PRESENT SERIES OF NINETY PATIENTS WITH ACUTE GLOMERULONEPHRITIS

TYPE OF INFECTION	NO. PATIENTS	PER CENT
Upper respiratory infection (pharyngotonsillitis, otitis media)	59	65.3
Skin lesions	9	10.2
Scarlet fever	3	3.3
Mumps	2	2.2
Gastrointestinal infections	2	2.2
Pneumonia	2	2.2
Adenitis	2	2.2
Sinusitis	2	2.2
Genitourinary infections	1	1.1
Syphilis	1	1.1
Unknown	7	8.0
Total	90	100.0

Etiologic studies were not carried out on every child, but beta hemolytic streptococci were found most frequently on throat culture while *Staphylococcus aureus* was usually the organism cultured from coexisting skin infections.

PRESENTING SYMPTOMS

Study of the presenting symptoms in this series constitutes an interesting analysis (Table III). Edema, as might be expected, was the outstanding symptom of 59.5 per cent of the patients. Next in frequency was gross hematuria which was the chief complaint of 25.5 per cent. Abdominal pain was present at one time or another in one-third of the patients; in six, comprising 7 per cent of the total number, it was the presenting and chief complaint. In several cases the diagnosis of appendicitis was entertained upon admission; especially in those

patients with nausea and vomiting; however, this pain was usually periumbilical or located in the right upper quadrant. In several patients its origin was probably a distended, congested liver with stretching of Glisson's capsule due to heart failure. Dyspnea was occasionally noted, especially in the group with demonstrable myocardial damage, and was the main complaint of two children upon admission. Convulsions and coma were the presenting symptoms in two other patients, and in another nephritis was diagnosed by routine urinalysis after the child was admitted with a diagnosis of pneumonia.

TABLE III. PRESENTING MANIFESTATION OF ACUTE GLOMERULONEPHRITIS IN CURRENT SERIES

MANIFESTATION	NO. PATIENTS	PER CENT
Edema	54	60.0
Hematuria	23	25.6
Abdominal pain	6	6.7
Vomiting	2	2.2
Convulsions	2	2.2
Dyspnea	2	2.2
Dysuria	1	1.1
Total	90	100.0

MAJOR MANIFESTATIONS

1. *Hematuria and Albuminuria.*—These two findings constituted the diagnostic criteria of acute glomerulonephritis and were present in every child. It is interesting to note that in at least three cases in this series, the impression of acute glomerulonephritis was entertained in view of the presence of several other manifestations of the disease, but the diagnosis was not definitely established until a second or third urine specimen revealed hematuria after twenty-four to forty-eight hours, the initial urinalysis showing no abnormalities of the urinary sediment. Red blood cells varied in amount. Gross hematuria was present in approximately one-fourth of the patients and microscopic hematuria was found in the remainder. The amount of albumin varied from 50 to 2,000 mg. per cent but the usual range was between 100 and 500 mg. per cent on initial urinalysis; the albuminuria disappeared in the majority of instances within four weeks after the onset of the initial symptoms. Casts were frequently noted. Daily examination of the urine was employed during the hospital course and reliance was placed on the correlation between the gradual disappearance of the urinary findings and the subsidence of the illness.

2. *Edema.*—Edema is the most common symptom of acute nephritis and was present in 84.4 per cent of the ninety patients in this series. It was not clinically perceptible in 16 per cent, was minimal in 37 per cent, moderate in 28 per cent, and severe in 19 per cent. The patients with nephritis without edema usually posed the diagnostic problems in this group. Edema usually developed in the face, particularly in the low tension tissues in the infraorbital region. It was often confined to this area, but frequently continued to develop, and appeared in the lower extremities and subsequently in all the subcutaneous tissues, serous spaces, and viscera. The patient who develops edema of the face only to have it disappear and then reappear later on, must be regarded

as a potential candidate for classification as having subacute or chronic nephritis. It is noteworthy that in all the patients in this series who went on to recovery, the edema was either progressive or came to a standstill, and was not intermittent.

TABLE IV. FREQUENCY OF OCCURRENCE OF MAJOR MANIFESTATIONS OF NINETY PATIENTS WITH ACUTE GLOMERULONEPHRITIS

MANIFESTATION	NO. PATIENTS	PER CENT
Hematuria	90	100.0
Albuminuria	90	100.0
Edema	74	84.4
Hypertension	73	81.1
Congestive heart failure	—	57.0
Abdominal pain	35	33.3
Cerebral symptoms	28	31.1

3. *Hypertension.*—Significant elevation of the blood pressure was present in 81.1 per cent of the children in this series. Arbitrarily, in agreement with other observers, systolic pressure of 120 was selected as the dividing line for the presence or absence of *significant* hypertension, although it is recognized that in young children, particularly those under the age of 5 years, a systolic pressure of 120 may well constitute hypertension.

At least one systolic blood pressure reading above 140 was observed in 44 per cent of the patients, and pressures ranging between 120 and 140 were observed in 30 per cent. The blood pressure was usually elevated at the time of admission, although in eleven children it never did rise while under observation. One child among this group without significant hypertension died of acute, nephritic, congestive heart failure shortly after admission. In nearly all patients showing marked cardiac manifestations a significant elevation of the blood pressure was noted. Marked hypertension as a sine qua non in the presence of congestive heart failure associated with acute glomerulonephritis has been the subject of some discussion. It was present in all of the fourteen cases of nephritic heart failure reported by Rubin and Rapoport.[6] On the other hand, Levy[7] and Lyttle[2] have reported cases in which this association was not observed. In the present series, three patients with heart failure did not have significant blood pressure elevation.

Occasionally, the blood pressure was noted to rise considerably after admission, particularly in those children who were admitted to the hospital at the very onset of the illness. However, in the majority of instances the highest readings observed were at the time of admission and under treatment they fell, over a period of one to two weeks, to normalcy. The systolic pressure was found to be a reliable guide to the degree of hypertension, and in most instances the diastolic pressure followed the systolic; however, in a few cases the systolic pressure remained within relatively normal range while an elevated diastolic pressure was observed. It is probably fair to assume that if all patients with acute glomerulonephritis could be adequately followed from the very first day of their illness during the entire course, a larger percentage might show a significant hypertension.

4. *Cerebral.*—Cerebral symptoms in this disease are probably caused by vasospasm with secondary cerebral ischemia. Vasospasm is probably also the cause of the hypertension. The evidence would indicate that cerebral edema plays an unimportant role in the etiologic background of the manifestations of encephalopathy associated with acute glomerulonephritis.

Cerebral symptoms in this series were present in 31.1 per cent of the patients. All of these patients had severe headaches, convulsions, or were in coma. These three symptoms were the diagnostic criteria employed and an associated moderate or severe hypertension was usually present. In general, these symptoms indicate a severe type of acute glomerulonephritis. Some of the other patients manifested cerebral symptoms of a milder degree such as slight headaches, restlessness, and dimness of vision.

5. *Cardiac Manifestations.*—It has long been known that cardiac failure may complicate the early stages of acute glomerulonephritis. In 1879 Goodhart[8] called attention to this association, and since then many reports have appeared on the subject in the literature. Of particular note is Whitehill and associates'[9] carefully studied series of 138 young adults with acute nephritis, ninety-eight, or 71 per cent, of whom showed clinical evidence of cardiac insufficiency. Forty per cent of eighty patients reported by Marcolongo[10] and 33 per cent of the twenty-four patients reported by Master and associates[11] exhibited cardiac failure. Lyttle[2] states that one-half of the 125 children with acute nephritis studied at Babies' Hospital in New York demonstrated cardiac failure, while fourteen of the fifty-five children with acute glomerulonephritis observed by Rubin and Rapoport[6] had congestive heart failure associated with the disease.

Acute glomerulonephritis has been the most common cause of congestive heart failure at Children's Hospital for the past three years, during the period covered by this series, and was present in thirty-five or 57 per cent of the sixty-two patients who were examined for evidence of this complication. The criteria used to diagnose heart failure were: (1) cardiac enlargement with congestion of the parenchyma as revealed by x-ray; (2) elevated venous pressure (using 160 mm. of normal saline as the maximal normal level) with a significant rise upon moderate pressure over the right upper quadrant; (3) engorgement with definite enlargement of the liver; and (4) miscellaneous evidence including electrocardiogram changes, pulsating cervical veins, pulmonary edema, dyspnea, and direct evidence at autopsy.

Some patients had definite evidence of cardiac dilatation by x-ray which returned to normal size while under observation, but confirmatory evidence of an elevated venous pressure and palpable liver was lacking, so these were not considered to be patients with congestive failure. However, if transient dilatation may be interpreted as evidence of partial impairment of cardiac function and these patients are grouped with those exhibiting frank congestive failure, then a total of 72.6 per cent of the sixty-two patients who were examined for evidence of this manifestation had demonstrable myocardial damage with insufficiency.

The signs of congestive heart failure were present usually in the first

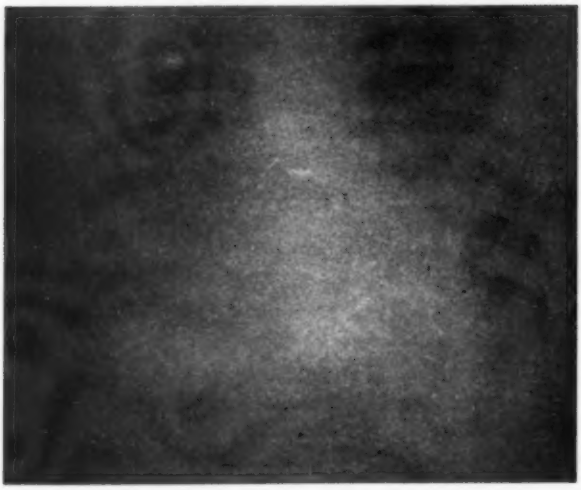


Fig. 1, *A*.

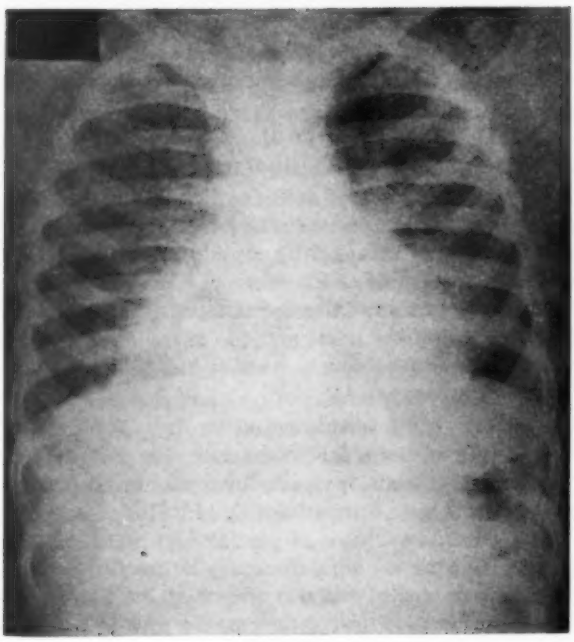


Fig. 1, *B*.

(For legend, see opposite page.)

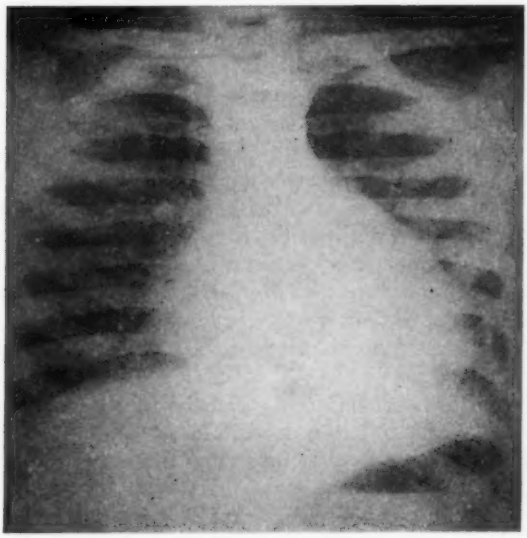


Fig. 1, *C*.

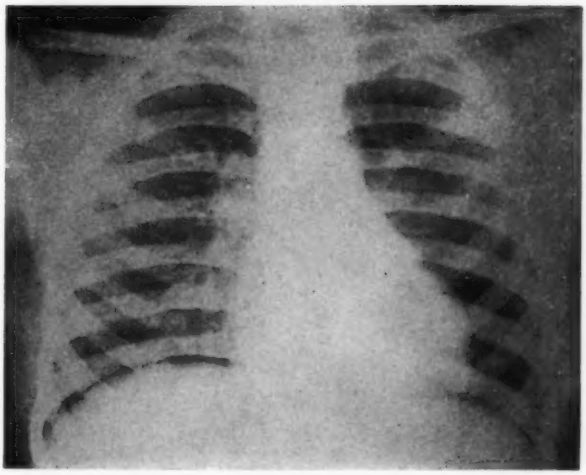


Fig. 1, *D*.

Fig. 1.—(C. K.) Serial roentgenograms of the chest demonstrating congestive heart failure associated with acute glomerulonephritis.

A, x-ray upon admission, shows the transverse diameter of the heart to be within normal limits but considerable congestion throughout the parenchyma. Venous pressure was elevated.

B, dilatation of the heart is shown on the picture taken fifty-six hours later with the congestion disappearing from the outer thirds of the lung fields. Venous pressure was still elevated. The patient was receiving digitalis.

C, further dilatation is noted on the x-ray taken four days after admission. Digitalization has been maintained, and venous pressure is normal. Congestion of the lungs is absent.

D, three weeks after admission, the heart is normal.

week after the appearance of the initial symptoms of acute glomerulonephritis. Most commonly these signs were detected upon admission; however, in several patients it was possible to demonstrate by serial roentgenograms a delay of two to three days before significant enlargement occurred.

Figs. 1 and 2 represent sets of teleoroentgenograms selected from the group showing classic evidence of congestive heart failure and illustrate the marked transient quality of decompensation due to acute glomerulonephritis.

A transient diastolic murmur at the base was observed in one patient with very severe decompensation and was interpreted as evidence of functional aortic regurgitation; this murmur disappeared when compensation occurred. Functional, apical, systolic murmurs were frequently noted but appeared to have no particular significance. Gallop rhythm was observed in five patients and is always to be regarded as a grave prognostic sign. It was present in two of the three patients who died.

The mechanism of heart failure associated with acute glomerulonephritis is not exactly known, but it is probable that there are several factors concerned with its production. The two most important of these appear to be hypertension due to vascular spasm, and toxic changes in the myocardium probably vascular in origin but independent of hypertension. Elevation of the blood pressure may represent a trigger mechanism which tips over a damaged heart into congestive failure. While the vast majority of patients showing congestive

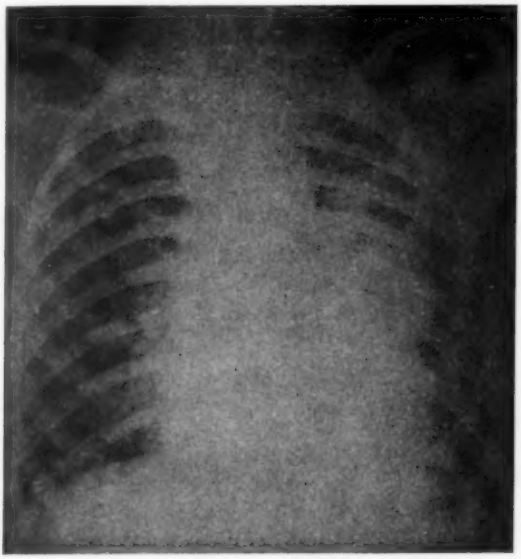


Fig. 2, *A*.

Fig. 2.—(S. S.) Serial roentgenograms of the chest.

A, Cardiac dilatation with parenchymal congestion especially marked on the left side. The venous pressure was very high and the patient was digitalized.

B, X-ray taken three days later showing a clearing of the lung fields with cardiac dilatation. The venous pressure was still slightly elevated.

C, Sixteen days after the first x-ray was taken, demonstrating a normal heart contour.

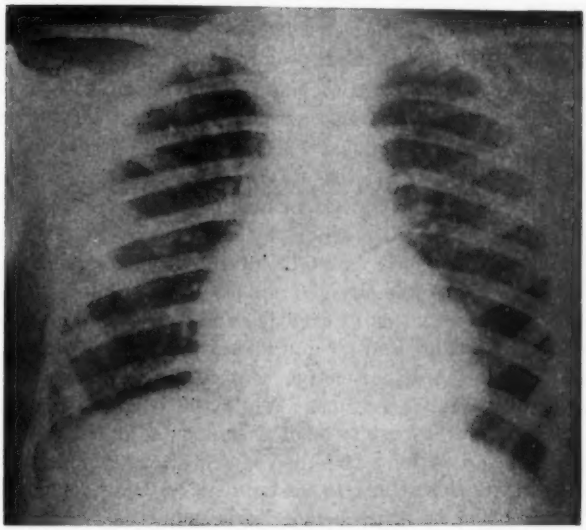


Fig. 2, *B*.

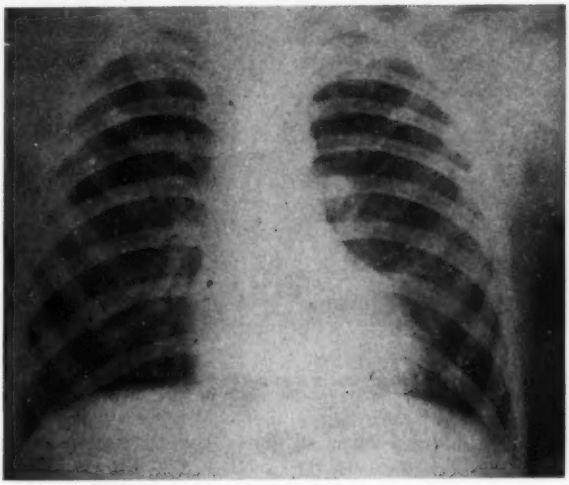
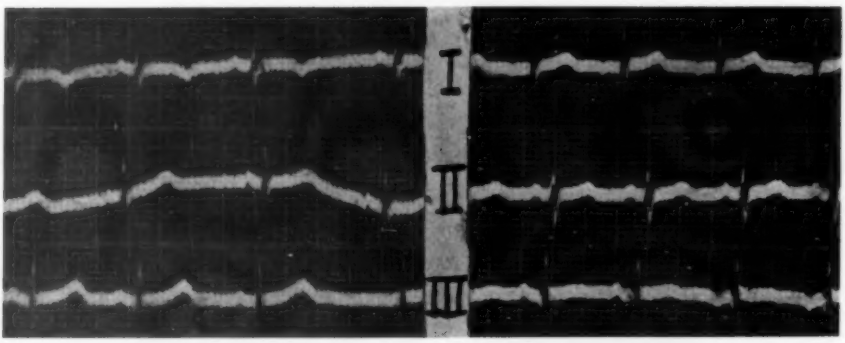


Fig. 2, *C*.

(*For legend, see opposite page.*)

heart failure had an associated elevation of blood pressure (95 per cent), it is worth while to note that three failed to demonstrate any significant elevation of pressure. One of these three died of congestive heart failure with a blood pressure of 110/55. Although the absence of hypertension in the presence of congestive heart failure associated with acute glomerulonephritis is relatively infrequent, the finding of even a few cases would suggest the importance of the role of underlying myocardial damage. The nature of this factor is not clearly understood. The theory that the disease represents a toxic, generalized capillaritis of the entire vascular system including the myocardium with associated temporary damage is still accepted by most observers at the present time. Longcope and associates[12] have pointed out the intimate relationship existing between infections due to hemoltyic streptococci and the subsequent onset of acute nephritis. The association of cardiac damage with streptococcal infections is well known. Brody and Smith[13] found heart lesions of varying degrees of severity at autopsy in more than 90 per cent of the patients with scarlet fever and related streptococcal infections. While the common myocardial lesions described in scarlet fever appear to be of an inflammatory nature, changes noted in the cardiac muscle of patients who died of acute hemorrhagic nephritis appear to be of a degenerative character. It has been suggested by Rubin and Rapoport[6] that if the renal lesion in acute hemorrhagic nephritis is anaphylactoid, it is possible that the cardiac involvement may be of a similar etiology.



A. *B.*

Fig. 3.—*A*, Electrocardiogram taken upon admission showing inverted T waves in Lead I. *B*, Normal record noted on check-up two months later.

Electrocardiographic evidence supports the theory of actual myocardial damage. Electrocardiograms were taken at random intervals during the course of the disease in thirty of the patients in the present series, and abnormal records were found in thirteen (43 per cent). The most common abnormal changes found were the flattening or inversion of the T waves, especially T_1 and T_2 (Fig. 3). Follow-up studies revealed that the myocardial damage was only temporary; all of the records were normal within two to four weeks after the onset of the nephritis in those patients who had shown abnormal readings

initially. It is a fair assumption that if serial electrocardiograms had been taken in all cases, a larger percentage of abnormalities would have been recorded. Ash and associates[14] found significant variations in 72 per cent of fifty children with acute nephritis, by employing the serial method.

MINOR MANIFESTATIONS

Anemia of varying degrees of severity was a rather frequent finding, and was marked (hemoglobin 8 Gm. or less) in 20 per cent, and moderate (hemoglobin between 9 and 10 Gm.) in 52 per cent of the cases.

Anuria was not observed in any instance, but oliguria was noted not infrequently in the first few days of illness. The nonprotein nitrogen blood level was above 35 mg. per cent in 65 per cent of the cases and was normal in the remaining 35 per cent.

Fever was not characteristic of acute glomerulonephritis and was absent upon admission in 60 per cent of the cases. When an elevation of the temperature was present, an associated extranephritic infection could usually be simultaneously demonstrated.

A rapid sedimentation rate was a rather constant feature of nephritis during the acute phase of the disease.

PROGNOSIS AND RESULTS

Eighty-four or 93.4 per cent of the patients in this series recovered while three (3.3 per cent) died during the acute attack. Three developed chronic glomerulonephritis and one of these patients died several months later of pneumonia. All of the patients who recovered have remained well in a follow-up period varying from a few months to two years. In no case was there any residual cardiac damage demonstrable.

TABLE V. OUTCOME IN NINETY CASES OF ACUTE GLOMERULONEPHRITIS

OUTCOME	NO. PATIENTS	PER CENT
Recovered	84	93.4
Died	3	3.3
Chronic	3	3.3
Total	90	100.0

A recrudescence of the symptoms of acute glomerulonephritis, particularly hematuria and albuminuria, may be precipitated by secondary acute upper respiratory infections or by one of the common contagious diseases acquired during the convalescent period. This, however, cannot be considered as a second attack of acute glomerulonephritis but rather as an exacerbation of the original disease process, nor does such an exacerbation necessarily predicate a bad prognosis. In two such instances a recurrence of albuminuria and hematuria was noted during the convalescent period after apparent recovery; in one of these patients mumps was the complicating secondary infection and in the other, chickenpox. However, in both cases the urinary abnormalities subsided within three to four weeks and the patients went on to complete recovery.

The low incidence of chronic nephritis as a complication is in accord with several other reports. Three patients developed chronic glomerulonephritis

after an apparently acute onset, and very early in the course of their disease showed large amounts of albumin in the urine out of proportion to the number of red cells. This disproportion of albuminuria to hematuria was regarded as a significant prognostic indication of the development of chronic nephritis. The high incidence of subacute and chronic glomerulonephritis following acute glomerulonephritis reported in adults[9] has not been observed in this series of children.

The onset and presenting symptoms of one of the patients who went on to chronic glomerulonephritis were indistinguishable from those of patients who completely recovered. However, early in the course of the disease this child showed a gradual disappearance of red cells from the urinary sediment, associated with increasing amounts of albuminuria. At the end of a one-year follow-up period, there was still between 2,000 and 3,000 mg. per cent of albumin in the urine with but an occasional red blood cell. Symptomatically, his course has been characterized by exacerbations and remissions of generalized edema.

A second patient who went on to the chronic nephritis and subsequently came to autopsy, had a history of intermittent edema of the face for three weeks prior to admission. This patient had, upon admission, very large amounts of albumin ranging between 2,000 and 4,000 mg. per cent with relatively few red blood cells. These findings persisted until death, four months after the onset of the disease, due to an intercurrent pulmonary infection.

The persistence of albuminuria with or without hematuria for a period of one year can usually be regarded as indicative of the presence of subacute or chronic nephritis.

No definite correlation could be established between the apparent severity of the clinical picture upon admission and the ultimate prognosis. Two of the three fatal cases were thought to be only moderately ill upon admission, whereas several patients in this series presented a much more severe initial clinical picture and yet ultimately recovered.

The most common cause of death in acute glomerulonephritis in children is congestive heart failure. The three deaths in this series were the results of or were associated with this complication. However, when it is considered that 72 per cent of the patients evidenced clinical signs of myocardial involvement, the mortality rate (3.3 per cent) is relatively low.

Addis counts on the urinary sediments, erythrocyte sedimentation rates, and observation of serial urea clearance tests are valuable adjuncts during convalescence in determining the prognosis. Concentration and dilution tests, phenolsulfonphthalein excretion tests, and intravenous pyelography were employed in a few patients but were discarded as routine procedures because they provided no additional information.

TREATMENT

Treatment consisted of absolute bed rest until the urine was free from albumin and red blood cells. Several cases were discharged before the urinary sediment was completely normal when it was felt that the convalescence would be intelligently followed at home. When patients were permitted premature

exercise, exacerbations of albuminuria and hematuria were noted on several occasions.

A relatively high protein, high carbohydrate, low fat, salt-free diet was employed with fluids given as desired. In those cases showing a high nonprotein nitrogen, fluids were forced. High vitamin supplements were employed routinely. Blood transfusions were given only when convalescence was well advanced and the initial phase of the attack had subsided. It was thought advisable to avoid the intravenous route in a disease with acute and generalized vascular involvement such as nephritis. In two instances when blood transfusions were given during the first few days after the onset of the symptoms of nephritis, gross hematuria ensued shortly thereafter.

Sulfadiazine, sulfapyrazine, and penicillin were employed when a susceptible infection was concomitantly present, without any untoward reaction being noticed. Penicillin appears to be the drug of choice for the treatment of such coexisting extranephritic infections, since, in the presence of impaired renal function, sulfonamides may be retained with the production of an inordinately high sulfonamide blood level. Regarding the use of chemotherapeutic agents for the treatment of nephritis per se, Rapoport and associates[15] found no appreciable difference in comparison of a series of thirty-three patients with acute glomerulonephritis treated with sulfonamides, with a control group of forty patients who were not treated with this drug. Similarly, penicillin cannot be expected to influence significantly the course of acute glomerulonephritis.

Magnesium sulfate (0.2 c.c. per kilogram body weight of a 25 per cent solution) was given intramuscularly in those cases manifesting cerebral symptoms or in those patients who showed a rising blood pressure. This dosage was repeated every two to four hours until hypertension was under control and/or signs of cerebral encephalopathy disappeared. The intramuscular route was found adequate and in no instance was the magnesium sulfate given intravenously. It has been shown that this drug exerts its beneficial effect on hypertensive encephalopathy associated with acute glomerulonephritis due to the relaxation of the arterial spasm rather than to the production of diuresis with diminution of the degree of cerebral edema. The magnesium ion has a relaxing effect on this vasospasm.[16]

Surgical procedures were not contraindicated by the presence of acute glomerulonephritis when they were deemed advisable, but elective operations were deferred. Hypertonic solutions were given to several patients in an attempt to mobilize the edema without success. Mercurial diuretics were not employed because of the potential harmful effect of these drugs upon an already damaged kidney. Xanthine derivatives did not appreciably hasten diuresis in the several cases in which they were employed. Intake-output records were discarded as a tedious and unreliable procedure in children, and equally valuable information was obtained by daily weighing and observation of the resultant weight curve. Only a few of the patients in the early part of this series were digitalized; however, in the later group, the majority received digitalis for the treatment of congestive heart failure. While it is true that most patients with congestive failure due to acute nephritis will respond to bed rest alone for re-

pair of their cardiac function, it is considered advisable to digitalize all patients with decompensation because of its possible serious import. In contrast to the deleterious effect of digitalis frequently noted in patients with acute rheumatic myocarditis, no untoward reactions were noted in the group of nephritic heart failure cases who received this drug. The preparation of choice was Digifolin and one cat unit per 100 pounds of body weight were employed. One-half the total dose was administered the first day in three divided doses, then one-half of the remainder on the second day in two doses and the rest on the third day. A maintenance dose of ½ cat unit every day followed until evidence of heart failure had disappeared or toxic symptoms intervened.

CONCLUSIONS

1. A review of the salient clinical features of ninety consecutive cases of patients with acute glomerulonephritis observed at the Children's Hospital during the past three years (1943 through 1945) is presented. The presenting symptoms and clinical manifestations are noted.

2. Of this series, eighty-four patients or 93.4 per cent recovered, while three (3.3 per cent) died during the acute attack. Three (3.3 per cent) developed chronic glomerulonephritis. The three deaths were associated with or were the direct result of acute nephritic congestive heart failure.

3. Acute glomerulonephritis has been the most common cause of congestive heart failure at Children's Hospital for the past three years, and was present in thirty-five or 57 per cent of the sixty-two patients with acute nephritis who were examined for evidence of this complication.

4. The treatment employed in this series is indicated and consisted largely of absolute bed rest and the management of symptoms as they appeared. The advisability of administering digitalis to all cases of acute nephritis complicated by congestive heart failure is suggested.

We wish to express our appreciation to Drs. Joseph S. Wall, E. Clarence Rice, P. A. McLendon, and Edgar Copeland for their helpful suggestions and advice. Dr. Bernard J. Walsh was the cardiac consultant and gave valuable aid and suggestions in those cases demonstrating heart complications. Dr. Charles Webb assisted in the compilation of statistics.

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THE AGGLUTINATIVE REACTION FOR HEMOPHILUS PERTUSSIS FOLLOWING WHOOPING COUGH AND FOLLOWING IMMUNIZATION

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NUMEROUS attempts have been made in the past to devise a simple and reliable test for differentiating persons immune and nonimmune to pertussis. The agglutinative reaction has been compared with other tests, such as complement fixation reaction, opsonocytophagic response, mouse protection test, and skin test in rabbit and man. According to Mishulow and associates,[1] the high agglutinin titer observed during the active stage of whooping cough decreases rapidly with the onset of convalescence. Miller and Silverberg[2] and Lapin[3] found that the agglutinin titers were higher and persisted for a longer period following immunization than after pertussis. The response following a stimulating dose of pertussis vaccine was studied by Wu and Chu,[4] who noted an eight to sixty-four fold increase of the agglutinin titers one to two weeks after a booster dose given four to nineteen weeks after the last dose of the original immunization. In Lapin's series,[5] the agglutinin titer two weeks following a stimulating injection of pertussis vaccine showed a more than twofold increase.

Additional information concerning the degree and persistence of the agglutinin response following pertussis, after administration of various vaccines and "antigens" and after a booster dose of pertussis vaccine, are presented in this communication.

MATERIAL AND METHODS

Sera.—Blood samples from 130 children (65 males and 65 females, 1 to 12 years old) attending the Pediatric Clinic were collected in sterile Pyrex centrifuge tubes, kept at room temperature for one hour, and then centrifuged at 1,500 r.p.m. for fifteen minutes. The clear serum was transferred to a sterile Pyrex test tube and stored in an ice box at 4 to 6° C. until tested, usually within one to two weeks after the withdrawal of the blood.

Antigen.—In preliminary tests, a commercially available, colored suspension of killed pertussis bacilli,* diluted to a density of approximately 4 billion organisms per milliliter, was compared with a bacterial suspension prepared from phase I Hemophilus pertussis† and diluted to an equal density. Since the results with the two antigens were identical, the former was used in this study.

From the New York Hospital and the Department of Pediatrics, Cornell University Medical College.

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*The antigen was purchased from the manufacturer, Eli Lilly and Co.

†Obtained through the courtesy of Miss L. Mishulow of the Department of Laboratories, Health Department of New York City.

Agglutination Reaction.—Serial twofold dilutions, 0.5 ml. volumes in physiological saline solution of the sera, ranging from 1:5 to 1:5,120, were mixed with an equal amount of freshly diluted antigen, the final serum dilutions thus ranging from 1:10 to 1:10,240. The mixtures were made in 12 × 100 mm. test tubes, shaken by hand, and incubated overnight in a water bath at 55° C. Readings were made the next morning and the last tube in which agglutination was visible with the naked eye was recorded as the titer. If agglutination was absent or present only in a final dilution of 1:10, the result was considered negative. Agglutinations in final serum dilutions of 1:20 to 1:80 were considered as evidence for the presence of agglutinins in a "low" titer. Agglutination in dilutions of 1:160 or more were arbitrarily designated as "high" titer. The following controls were used: (1) each serum tested plus saline; (2) the bacterial suspension plus saline; (3) serial dilutions of an antipertussis rabbit immune serum plus bacterial suspension; (4) normal rabbit serum plus bacterial suspension. In every instance, control series (3) was positive; the other controls were negative. In addition, a microscopic slide agglutination reaction (Powell and Jamieson[6]) was carried out routinely.

RESULTS

A. Children With a History of Pertussis.—The agglutinin titer of thirty-eight children was determined one-fourth to eleven years after a history of the disease. A high titer was found in five (13.2 per cent) after an interval between disease and testing ranging from three-fourths to eight years. A low titer was present in eight (21.0 per cent), who had had pertussis one-fourth to eight years before testing. In the remaining twenty-five (65.8 per cent) the agglutination reactions were negative. These children gave a history of pertussis or of a pertussis-like disease, two to eleven years prior to testing. A graphical presentation of the results obtained in this and in the following groups is given in Fig. 1.

B. Children Injected Prophylactically With Full Courses of Pertussis Vaccines.—Of the forty-six children in this group, thirty-three had received the Sauer Vaccine (Parke, Davis & Co.) and the remaining thirteen had been given various other commercially available pertussis vaccines (Cutter's D-P-T, Lederle's, Lilly's, and New York City Board of Health's vaccines). Usually, a total of ninety to 100 billion killed microorganisms was administered subcutaneously, given with an interval of four weeks between the three injections. The agglutination reaction was negative in three (6.5 per cent), a low titer was noted in ten (21.8 per cent), and the remaining thirty-three (71.1 per cent) had agglutinins in high titers (Fig. 1). The time interval between the last injection and testing for agglutinins ranged from six weeks to nine years and is presented in Fig. 2.

C. Children Injected Prophylactically With Full Courses of Pertussis Antigen.—A full course of three subcutaneous injections of 1 c.c. (with an interval of three weeks between injections) of Tri-Immunol,* "a bacterial vaccine made

*Obtained through the courtesy of Lederle Laboratories, Inc.

from diphtheria toxoid, tetanus toxoid and pertussis antigen," was given to twenty-four children and their agglutinin response studied six to eighteen months later. Negative results were found in eight (33.3 per cent), a low titer in fourteen (58.4 per cent), and a high titer in two (8.3 per cent) (Fig. 1).

D. Controls With No History of Pertussis or Prophylaxis.—The sera of seventeen children were tested. A low agglutinin titer was found in one; the others were negative (see Fig. 1).

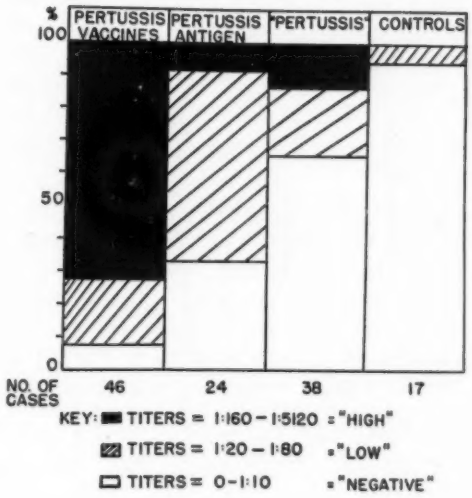

Fig. 1.

E. Children Injected With a Stimulating Booster Dose of Pertussis Vaccine.—Of the thirty-nine children in this group, nine gave a history of pertussis (group A), five had received pertussis vaccines (group B), and twenty-five had received pertussis antigen (group C). In five of these children, no agglutination reactions were made prior to the administration of the booster dose. The results are presented in Table I.

TABLE I. EFFECT OF "BOOSTER" INJECTION OF PERTUSSIS VACCINE ON AGGLUTININ TITER

PREVIOUS HISTORY	NUMBER	TITER* BEFORE BOOSTER INJECTION			INTERVAL BETWEEN BOOSTER AND AGGLUTININ TEST (WEEKS)	TITER* AFTER BOOSTER INJECTION		
		NEGATIVE	LOW	HIGH		NEGATIVE	LOW	HIGH
Pertussis	9	7	2	0	6-10	0	5	4
Vaccine injections	5	3	1	1	6-20	1	0	4
Antigen injections	20	7	11	2	4-16	0	5	15
Antigen injections	5	not tested			8-12	0	2	3

*Number of sera that were negative or had a low or high agglutinin titer.

F. Comparison of Slide Agglutination With Test Tube Agglutination.—The slide and test tube agglutination reactions were compared in 191 experi-

ments. The results are summarized in Table II. They show that the slide agglutination method alone may not differentiate between low and high agglutinin titers.

TABLE II. COMPARISON OF AGGLUTININ TITERS OBTAINED BY SLIDE AGGLUTINATION WITH THOSE OBTAINED BY TEST TUBE AGGLUTINATION

SLIDE AGGLUTINATION	NUMBER	NUMBER OF SERA IN TEST TUBE AGGLUTINATION		
		WITH NEGATIVE TITER (0-10)	WITH LOW TITER (20-80)	WITH HIGH TITER (160 OR MORE)
Negative or doubtful	73	53	20	0
Weakly positive	33	0	23	10
Moderately positive	63	0	21	42
Strongly positive	22	0	0	22
Total	191	53	64	74

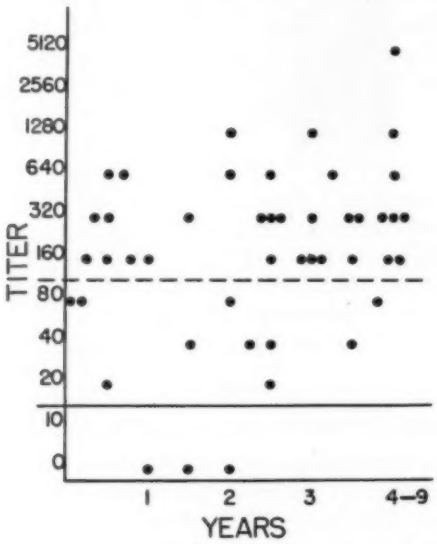

Fig. 2.

DISCUSSION

Our results indicate that agglutinins for H. pertussis can be detected in the serum of approximately one-third of the patients (34.2 per cent) for as long as eight years following the disease. This low incidence of positive response may be due in part to the difficulty of differentiating between true H. pertussis and H. parapertussis infection from the history, but in any case it would appear that the agglutinative reaction is of limited value in determining the state of immunity of an individual who allegedly had pertussis.

On the other hand, prophylactic injections with pertussis vaccines were followed by the appearance of agglutinins in forty-three of forty-six instances (93.5 per cent), and in thirty-three the titers were high and remained high for years, the longest observation being nine years postimmunization. Of the three

children who had no agglutinins, two had been given prophylaxis by their own physicians. All three were given stimulating injections, and two developed agglutinins in a high titer, while the third did not. This was the only failure in the group, and is unexplained.

In contrast to the consistently positive results in the vaccine group, of twenty-four children injected with "antigen," only two developed agglutinins in high titer; but Tri-immunol contains only a pertussis antigen obtained "after removal of the bacteria in the Sharples centrifuge and separation of the filtrate in the Berkefeld filter." Therefore, little if any agglutinin production should be expected in this group. The high titers observed in two children may be explained by the fact that the antigen might have contained sufficient antigenic components of H. pertussis bacilli to elicit an occasional marked agglutinin response, or by an anamnestic reaction to an undiagnosed pertussis infection in the past.

As far as we were able to ascertain, only two cases of pertussis occurred among those children of this study who received prophylaxis. They were siblings. One had received vaccine injections by his own physician but did not develop antibodies. A stimulating booster dose of vaccine was given to this child in our clinic but it also failed to elicit agglutinins (this was the only failure previously mentioned). The second child had been given pertussis antigen and had developed agglutinins in a low titer (1:80); a stimulating booster dose of vaccine raised the agglutinin titer slightly (from 1:80 to 1:160). The data are, therefore, inadequate to correlate agglutinin production with the state of immunity. However, our immunologic results may be compared with interesting clinical observations recently published by Cravitz and Cauley. These authors found that only 9.2 per cent of exposed Sauer-immunized children contracted pertussis, while 67.2 per cent of those who had received prophylaxis with the Lederle Detoxified Pertussis Antigen contracted pertussis upon exposure. Since the antigen used for prophylaxis in group C of this study was presumably identical to the one used by Cravitz and Cauley, the combined evidence suggests that bacterial vaccines confer high agglutinin titers and immunity, while administration of "antigens" does not. The presence of agglutinins in immunized persons may thus signify the existence of immunity to pertussis as suggested previously by Miller and associates.[8]

Stimulation of the antibody production by a single booster dose of a potent vaccine was successful in thirty-three of thirty-four attempts. The titers of seventeen children were negative at the time the booster dose was given. After the stimulating injection, low titers were found in seven, and high titers in nine children (one child's titer remained negative, as previously mentioned). The titers of fourteen children were low at the time the booster dose was given. They rose from 1:20 or 1:40 to 1:80 in three instances, and to high titers in the other eleven children (three to sixty-four-fold increases). Twofold to fourfold increases of the titers were found in three children who had high titers at the time of injection with the booster dose.

SUMMARY AND CONCLUSIONS

1. The agglutinative reaction for H. pertussis was found to be positive in 34.2 per cent of children who had a history of pertussis. The longest interval between recovery from the disease and testing with positive result was eight years.

2. Following prophylaxis with bacterial vaccines, agglutinins were found in 93.5 per cent; some of the determinations were made as long as nine years after immunization.

3. Prophylactic injections of "pertussis antigen" were rarely followed by high agglutinin titers.

4. Stimulating injections of pertussis vaccines evoked a notable rise of circulating agglutinins in 97.4 per cent.

5. There was some correlation between the results obtained by slide agglutination and test tube agglutination, but the slide test alone did not always differentiate between low and high agglutinin titers.

6. Of seventeen untreated control patients, sixteen had no agglutinins and one had agglutinins in low titer.

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INTRAVENTRICULAR BLOCK IN MALNUTRITION AND VITAMIN B DEFICIENCY

A Report of Two Cases in Children

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ELECTROCARDIOGRAPHIC changes due to vitamin B deficiency have been repeatedly described in recent years. Weiss and Wilkins,[12] in an extensive study on vitamin B_1 deficiency, found the most common changes to be depression and inversion of T waves and prolongation of the electrical systole. At times, low voltage of the ventricular complexes and premature beats were found. Similar electrocardiographic alterations in vitamin B_1 deficiency have been reported by other authors.[1, 4, 5, 7] The administration of thiamine chloride resulted in abolition of these electrocardiographic abnormalities. Changes in the electrocardiogram have also been described in pellagra. The abnormalities in pellagra are similar to those found in B_1 deficiency, and consist mainly in alterations of the T waves and the S-T segment.[2, 8] These changes are due specifically to niacin deficiency, since they disappear rapidly after treatment with niacin.[11]

In this paper, two cases of malnutrition and vitamin B deficiency are reported in children in whom an intraventricular block was found at the height of the deficiency and disappeared after treatment.

Case 1.—A 15-month-old boy was admitted to the Pediatric Department B on July 5, 1943, because of severe diarrhea and vomiting lasting a week. The child had always been poorly fed and had had diarrhea on previous occasions. On admission, he was markedly undernourished, and his weight was 6.300 kilograms (normal average, 11.000 kilograms). He was conscious but apathetic and did not react to his surroundings. Distinct signs of dehydration such as sunken eyeballs and plastic skin were present. The gums were red and swollen, the tongue was smooth and atrophic, the heart sounds were feeble. There were no abnormal findings in the lungs and abdominal viscera. During the first two days of his stay in the hospital there was no vomiting and no diarrhea. On July 7 diarrhea and vomiting recurred, and the child showed signs of acute dehydration and acidosis. An intravenous drip infusion of normal saline and 5 per cent glucose was installed. In addition, the child received daily 10 mg. thiamine chloride, 50 mg. niacin and one ampule of liver extract. The patient was also given a course of sulfathiazole by mouth since the diarrhea was considered to be of infectious origin. The intravenous infusion was discontinued after three days but medication with vitamins and sulfathiazole was continued. Later the child became more responsive and a general improvement gradually took place.

Electrocardiographic Examinations.—On July 6, the day following admission, the first electrocardiogram was taken, which showed the following changes: normal sinus rhythm; frequency, 80, P-R interval 0.2 sec., width of the ventricular complexes in the first lead 0.10 sec., in the second 0.20 sec., and in the third 0.20 sec. T waves were absent in the three limb leads (Fig. 1, *A*). On July 15 after nine days of treatment a second electrocardiogram was taken with the following results: normal sinus rhythm, frequency 88, right axis shift, P-R interval 0.17 sec. The width of the ventricular complexes was normal. T waves in the first and third lead were upright, in the second lead, isoelectric (Fig. 1, *B*).

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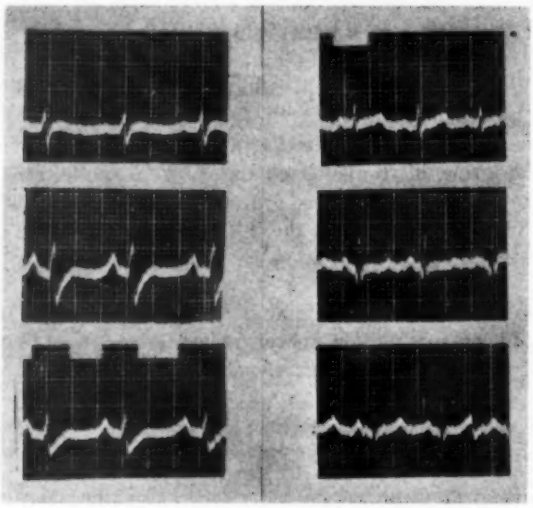
Thus we have before us a case of malnutrition and vitamin B deficiency with severe electrocardiograph changes and intraventricular block, which disappeared following a short course of treatment with vitamin B_1, niacin, and liver extract.

CASE 2.—A 5-year-old girl was admitted for the first time to the Pediatric Department A on July 3, 1945, suffering from severe diarrhea of three weeks duration. There was nothing of importance in her past or family history. On admission the child was markedly undernourished, her weight was 11.700 kilograms (normal average, 18.000 kilograms). There were no pathologic findings in the heart and lungs. The child had severe atrophic glossitis and edema of both legs. The stool was liquid and did not contain any parasites. The blood count was as follows: red blood cells, 3,550,000; hemoglobin, 60 per cent (Sahli), white blood cells, 6,500, with a normal differential count; total blood protein,

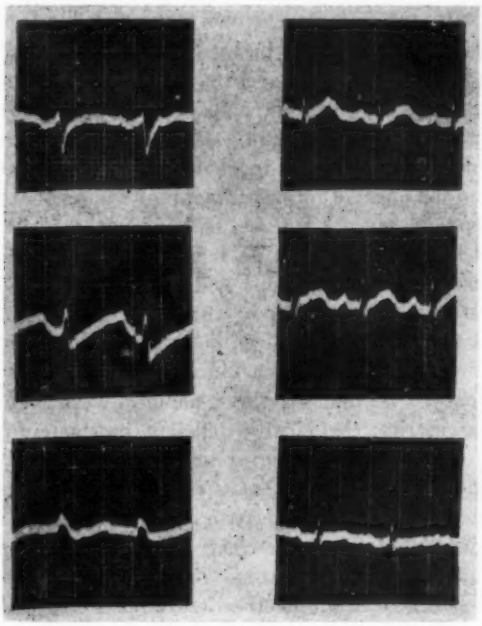


A. *B.*

Fig. 1.—*A*, first electrocardiogram on July 6, 1943, showing widened ventricular complexes and absent T waves. *B*, After nine days of treatment with vitamin B, niacin, and liver extract, the electrocardiogram is normal.

3.00 Gm. per cent; and albumin, 1.60 Gm. per cent. An intestinal infection was suspected and sulfaguanidine was given. The child received a diet rich in protein (protein milk), yeast tablets, and two blood transfusions. With treatment diarrhea gradually subsided and the general condition improved. The edema disappeared and on July 16 blood total protein went up to 6.1 Gm. per cent, and albumin to 4.05 Gm. per cent. On Aug. 9, 1945, the child was discharged in a good general condition. On Aug. 21 she was readmitted because of recurrence of the diarrhea. Again she was in a state of malnutrition (weight 11.350 kilograms), but this time no edema was noted. The tongue was smooth and fiery red. The total protein of the blood was 5.5 Gm. per cent. A course of sulfaguanidine was given again as well as yeast tablets and small amounts of niacin. On August 23, 165 c.c. of plasma were transfused. The treatment with yeast tablets was continued for three days, after which the child received niacin only (from August 21 to August 28, a total of 650 mg. niacin was given). Only slight improvement followed this treatment, and malnutrition was still present. A general and more comprehensive treatment consisting of liver extract, blood transfusion, vitamins, and concentrated diet was therefore instituted, resulting in gradual improvement in the patient's condition.

Electrocardiographic Examinations.—On the patient's first admission an electrocardiogram was made, which revealed isoelectric T waves in the first and second lead. During the second stay in the hospital three electrocardiograms were taken, between August 21 and August 28. The first showed the following: normal sinus rhythm, frequency 110, P-R interval 0.23 second (A-V block, first degree), widened ventricular complexes in the three leads (in the first lead 0.14 second, in the third lead 0.11 second; in the second lead the exact width could not be determined). T waves were undifferentiated in the three limb leads. This tracing resembled a right intraventricular block (Fig. 2, *A*). A second electrocardiogram taken on August 23 showed the same findings. A third electrocardiogram was taken on August 28. This was normal except for moderately low voltage of the ventricular complexes (Fig. 2, *B*).



A. *B.*

Fig. 2.—*A*, electrocardiogram on July 21 and July 23, 1945, shows prolongation of the P-R interval, widened ventricular complexes and absent T waves. *B*, electrocardiogram on July 28, after treatment with niacin only, is normal.

The electrocardiograph changes in this case were similar to those observed in the first one, the outstanding alterations being a prolongation in the intraventricular conduction time and abnormal T waves. All these changes disappeared completely after five days of treatment with niacin.

COMMENT

Both cases represent examples of reversible intraventricular block. This condition is rare and may be encountered in cases of acute heart failure, acute coronary insufficiency, acute infections, diphtheria, and digitalis overdosage. All these etiological factors could be excluded in our cases. Both patients had been suffering from prolonged diarrhea and were poorly fed. The clinical examination in both cases revealed, besides malnutrition, distinct evidence of

vitamin B deficiency (glossitis). In the first case the improvement in the electrocardiogram took place nine days after commencement of treatment with vitamin B_1, niacin, and liver extract, at which time the general condition of malnutrition was not yet affected. In the second case the disappearance of the electrocardiographic abnormalities was observed after five days of treatment with niacin only. It seems, therefore, that the vitamin deficiency was mainly responsible for the unusual and marked electrocardiographic abnormalities.

The changes described hitherto in human vitamin B deficiency were especially concerned with the T waves, which were flattened, isoelectric, or inverted. In vitamin B_1 as well as in niacin deficiency they were regarded as due to disturbed intracellular metabolism. The question arises as to whether such a marked change as an intraventricular block may be of metabolic origin, or whether it is caused by organic changes in the myocardium. It is generally accepted today that a deficiency state develops by stages. After the tissues become depleted of the specific nutrient, metabolic defects appear, and finally structural changes take place. Diffuse, isolated myocarditis associated with dietary deficiency has recently been described by Toreson.[10] The electrocardiogram in his case showed low and widened ventricular complexes. On autopsy, dilatation and hypertrophy of the heart and chronic, noninfective, inflammatory lesions of the myocardium were found. In animal experiments, focal and diffuse necrosis of the myocardium have been observed in pigs dying of thiamine deficiency.[3] Similar histologic changes have been noted by Hundley and associates[6] in rats chronically deficient in thiamine. These authors observed, besides other electrocardiographic changes, transient bundle branch block. In this study it was found that there was no conformity between the electrocardiographic changes and the pathologic findings. From previous observations[10] it appears that reversible electrocardiographic changes in pellagra were more marked in younger persons. The myocardium of young people seems to be more sensitive to metabolic disturbances than the myocardium of older individuals. May[9] made similar observations in studying the effect of anoxemia upon normal subjects. He reported that the degree of T-wave flattening was very high in young subjects and diminished greatly with advancing age. The rapid improvement of the electrocardiogram in our cases suggests that the abnormalities were due to metabolic disturbances affecting the intraventricular conductive system.

SUMMARY

In two children suffering from malnutrition and vitamin B deficiency, intraventricular block and abnormalities of the terminal deflection which disappeared following vitamin treatment were observed. The first patient received niacin, thiamine and liver extract, while niacin only was given to the second. These observations suggest that reversible intraventricular block may be caused by deficiency of the vitamin B complex.

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STREPTOMYCIN TREATMENT OF SALMONELLA ENTERITIS IN INFANTS

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EARLY observations by Waksman[1] and collaborators on the antibiotic action of streptomycin revealed the genus Salmonella to be one of the susceptible gram-negative organisms. Subsequent in vitro, in vivo,[2] and clinical[3] studies of the nature and activity of streptomycin repeatedly demonstrated its inhibitory effect on various Salmonella strains. An in vitro investigation of particular interest is the work of West and associates[4] who tested the susceptibility to streptomycin of 412 cultures of Salmonella, including all of the then known 154 serologic types, and found them to be inhibited in concentrations ranging from 2 to 23 units per milliliter. In view of the cases reported here it may be noted that these investigators found *Salmonella typhimurium* to be among the more susceptible strains.

We have recently had opportunity to observe several cases of *S. typhimurium* enteritis in the newborn.* This type of gastrointestinal infection is a more frequent cause of infantile diarrhea than is commonly believed. Though there are few comprehensive studies in the literature of Salmonella infections in infants, the observations recorded in recent large series of all age groups indicate that Salmonella gastroenteritis and its complications are an important pediatric problem. Thus, in analyzing 2,000 cases of human Salmonella infection, Seligmann and associates[5] report the occurrence of 17 per cent in infants and 40 per cent in children under 10 years of age. In this series as in a previous one of 1,000 cases,[6] the authors observed that the organism most commonly isolated was *S. typhimurium*, which occurred in more than 30 per cent of the infections reported.

Though the *S. typhimurium* usually remains restricted to the gastrointestinal tract, resulting in a mild diarrhea which is self-limited, fatalities due to secondary invasion producing septicemia, pneumonia, and meningitis, do occur. One outbreak involving seventeen infants with six deaths has been reported.[7] In view of the known streptomycin susceptibility of the organism and the possibility of preventing secondary invasion, it was decided to use streptomycin in treating five cases here reported.

CASE REPORTS

CASE 1.—B. H., a full-term male infant, was delivered by low forceps on May 16, 1946. There were no abnormal physical findings and the infant was fed a routine evaporated milk formula. During the first two days of life, meconium and apparently normal brown stools were passed. On the third day there was a sudden rise in temperature to 104° F.,

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The Streptomycin used in this study was supplied through the courtesy of Dr. Chester S. Keefer of the National Research Council, Committee of Chemotherapeutics and other agents.

*The epidemiology of this outbreak will be reported elsewhere.

associated with a diarrhea of eight green, mucoid stools in twenty-four hours. Supportive clyses were given and the feeding was changed to a low caloric, fat-free, protein milk formula. Temperature was normal on the following day and remained so during the entire course. There was no evidence of systemic involvement.

The stools were less frequent although still green and mucoid on the second day of illness. Stool cultures revealed infection with *S. typhimurium*. On the fifth day, streptomycin became available and was administered orally in 25 mg. doses every three hours for three days (total, 600 mg.). During the first day of therapy, stool culture was positive for the infecting organism, but on the second and third day the stool was sterile and the pathogenic as well as the fecal flora had been inhibited. However, on the day following cessation of therapy the stool was again positive for *S. typhimurium*. Infected stools persisted for three days when another course of therapy was instituted with an increase of oral dosage to 50 mg. every three hours for three days (total, 1,200 mg.). The stools were sterile during the first and second day of therapy on this dosage, and on the third day the pathogen could not be cultured from the stool though the normal fecal flora had returned.

The infant was now on an evaporated milk formula and the stools, although yellowish green, were of good consistency and frequency. To prevent cross contamination the infant was discharged but stools were received from home for culture. On the sixth day after discharge, stools were again positive for *S. typhimurium*. Three additional specimens taken over the following six days revealed a carrier state of *S. typhimurium*.

CASE 2.—F. P., a full-term male infant, was delivered by Barton and Simpson forceps on May 12, 1946. The immediate postnatal course was uneventful. On the third day of life eight green, mucoid stools were passed and the temperature rose to 104° F. The infant was starved for eight hours and a low caloric, fat-free, protein milk formula was fed. Adjuvant clyses were given. The temperature hovered between 101 and 102° F. for four days and the stools, although less frequent (four to five per day), were green and mucoid. Stool cultures on the third and fourth day after onset were positive for *S. typhimurium*. On the eighth day, 25 mg. of streptomycin were given orally, and repeated every three hours for three days (total dose, 600 mg.). On the second day of therapy the stool was sterile. However, four days after therapy was terminated the infecting organism had reappeared in the stool. Stool cultures remained positive for eight days thereafter at which time another course of treatment with dosage increased to 100 mg. of streptomycin orally every three hours for two days was begun (total, 1,600 mg.). On the second day of therapy the stool was sterile. The infant was discharged. Culture of a stool brought from home six days after the last dose of Streptomycin revealed the normal fecal flora. However, two days later *S. typhimurium* was again recovered from the stool. Specimens received on alternate days for a week continued to reveal the infecting organism.

CASE 3.—R. E., a full-term, normal infant, was delivered spontaneously on May 17, 1946. Physical examination was negative. The infant was breast fed. On the third day of life there was an unexplained rise of temperature to 101° F. which persisted for forty-eight hours. The stools were yellowish green but only three per day and of good consistency. In view of the existing outbreak, the stool was cultured and found to be infected with *S. typhimurium*. The infant was fed a diluted evaporated milk formula. There was no evidence of systemic illness. Streptomycin was administered orally 50 mg. every three hours for three days (total, 1,200 mg.). Stools cultured during the three days of medication as well as two days after the last dose were all sterile, and the infant appeared to be thriving. On the fifth day after the last dose of streptomycin, the stools became watery and frequent (nine in twenty-four hours) and culture revealed the recurrence of the infecting organism.

The infant continued to have a moderately severe diarrhea with positive stools for five days, at which time streptomycin again became available, and was administered orally in 50 mg. doses as well as intramuscularly in 25 mg. doses every three hours for three days (total, 1,800 mg.). After twenty-four hours of this combined oral and parenteral therapy there was no marked improvement and it became necessary to starve the infant for twenty-four hours

and administer intravenous fluids followed by feeding of gradually increasing amounts of fat-free, protein milk. The diarrhea subsided. On the third day of this combined therapy the stool was sterile, and remained so during the twenty-four hours after medication. The next day the normal fecal flora had returned. However, five days after medication the stool was again positive and remained so for three successive days.

CASE 4.—J. K., a full-term, normal, male infant, was delivered by Barton forceps on May 11, 1946. Examination revealed a left hydrocele and undescended testicle. On the second day of life the temperature rose to 102° F. There were no clinical findings. The temperature fluctuated between 102° and 103° F. on the following two days, and the stools were green, mucoid, and increasing in frequency (six in twenty-four hours). On the sixth day the temperature was normal and remained so but *S. typhimurium* was recovered from the stool. The infant was fed gradually increasing amounts of fat-free, protein milk and adjuvant clyses were given. The stools decreased in number (three to four per day) but continued to be green and mucoid. There were no evidences of systemic illnesses.

Until this time the infant had received no streptomycin as a control. Stools continued to be positive on the seventh, eleventh, fourteenth, fifteenth, and seventeenth days, at which time it was decided to institute therapy. Streptomycin was given orally in 50 mg. doses every three hours for three days (total 1,200 mg.). During the second and third day of therapy, stools were sterile. On the day after therapy, *S. typhimurium* reappeared in the stool. The infant was discharged on the twenty-third day. Stools from home cultured on alternate days for a period of one week continued to reveal the infecting organism.

CASE 5.—J. P., a normal, full-term, female infant, was delivered spontaneously on May 14, 1946. On the third day of life there were three, loose, watery stools associated with a temperature of 102° F. On the following day the temperature was normal although stools continued to be loose and frequent (eight in twenty-four hours). Stool culture revealed *S. typhimurium*. There was no evidence of systemic involvement. The infant was fed a gradually increasing fat-free, protein milk formula and adjuvant clyses were given.

This case remained untreated for two weeks and served as another control. Positive stool cultures were reported on the eighth, eleventh, fourteenth, sixteenth, seventeenth, eighteenth, and nineteenth days. On the nineteenth and twentieth days, streptomycin was given orally in 100 mg. doses every three hours (total 1,600 mg.). The stool was sterile on the second day of therapy as well as during the following twenty-four hours. Forty-eight hours later the pathogen recurred in the stool. The infant was discharged on the twenty-fourth day. Stools received from home on alternate days for one week following discharge were positive for *S. typhimurium*.

BACTERIOLOGY

The bacteriologic stool examination consisted of direct plating of the material on SS and Endo agar plates and seeding in Kauffmann's tetrathionate medium with subculture on SS plates after eighteen hours of incubation. Suggestive colonies were picked up for cultural and serologic tests. Identification of culturally typical cultures was performed by the use of group-specific O-sera and type-specific H-sera. In about 50 per cent of the specimens the suspected organism could be isolated from direct platings.

Studies on streptomycin activity against Salmonella organisms were begun in the bacteriologic laboratory of this hospital some months before the described outbreak occurred. M. Wassermann and one of us (E. S.), performed animal experiments and tested a great many different Salmonella cultures for their sensitivity to streptomycin in the test tube. Detailed results will be reported elsewhere. Of forty-one freshly isolated strains of *S. typhimurium*,

twenty yielded to 8 units of streptomycin, the rest to even smaller amounts (2 to 4 units). Thus, the relatively high sensitivity of this Salmonella type had been confirmed.

Cultures of *S. typhimurium* obtained from infants after discontinuation of treatment were tested in comparison with those isolated before the treatment started. No increased resistance was found; the reappearance of the Salmonella, therefore, cannot be explained by an acquired fastness of the organisms.

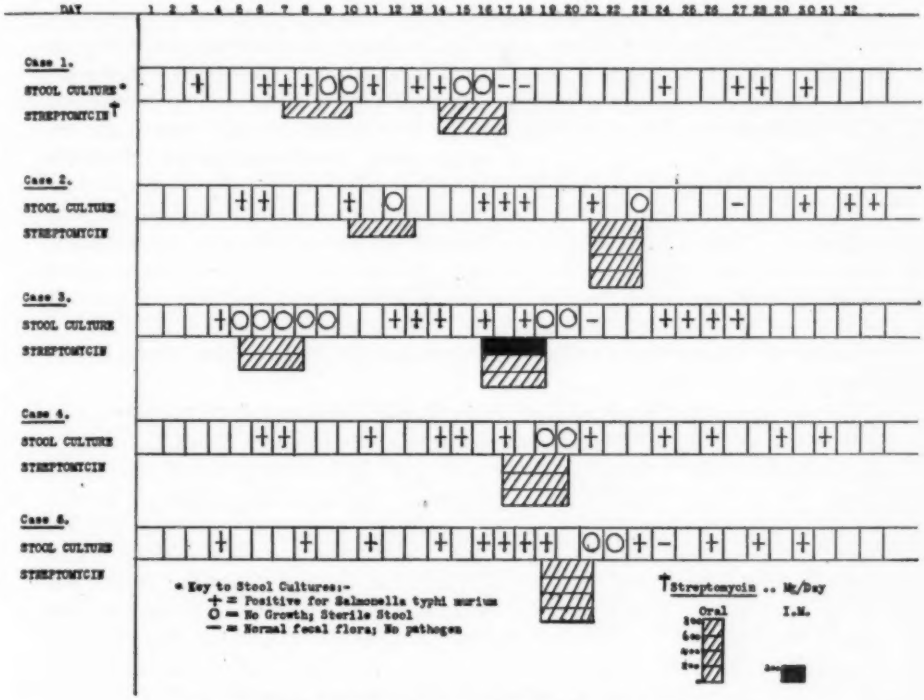

Chart 1.—Effect of oral streptomycin therapy on stool cultures.

The bacteriologic observations in infants are perfectly mirrored in previous animal experiments (Wassermann and Seligmann[11]). Mice, orally infected with *S. typhimurium*, received oral or combined oral and parenteral treatment with the following result. As long as the drug was given orally the stools were free of the normal fecal flora and pathogenic organisms. After discontinuation of treatment, *S. typhimurium* reappeared in the feces and the Salmonella infection ran its course. The bacteriostatic effect, definite as it appeared, was not able to turn to bactericidal action.

DISCUSSION

Studies of the absorption and excretion of streptomycin have demonstrated that the drug is not absorbed from the gastrointestinal tract in appreciable amount. After oral administration, only traces appear in the blood

and urine, for most is excreted unchanged in the feces in amounts more than enough to suppress susceptible organisms.[8] On the other hand, following parenteral administration, 40 per cent to 87 per cent of the drug is excreted in the urine within twenty-four hours; little, if any, is excreted in the feces.[9, 10] Inasmuch as in the five cases reported here we were dealing with an infection apparently limited to the gastrointestinal tract, the oral route appeared indicated.

Results as presented on Chart I reveal a distinct bacteriostatic action following oral administration of streptomycin. The effect, however, was only temporary. During and shortly after the ingestion of the drug, the pathogen as well as the normal flora were inhibited, resulting in sterile stools. However, in most instances within forty-eight hours, the pathogen, as well as the normal flora, reappeared. Repeating the treatment or increasing the dose again resulted only in temporary bacterial suppression. Inasmuch as not all stools were cultured daily, it is not always possible to state accurately the time interval between cessation of therapy and reappearance of the normal flora and the pathogen. Usually, stools remained sterile on culture for one to two days, after which normal growth was observed. *S. typhimurium* sometimes recurred twenty-four hours after the termination of medication; in other instances it reappeared from two to ten days later. There seemed to be no relationship between the total amount of ingested streptomycin and the time of reappearance of the pathogen.

In no instance did there seem to be any evidences of drug toxicity, even with doses as high as 800 mg. of streptomycin daily (Cases 2 and 5). Due to the limited supply of the drug, it was not possible to observe the effect of even larger doses over a longer period of time. However, the course of Case 3 merits added attention. The stools of this infant were rendered sterile for five days, beginning with the first day of the initial course of 400 mg. daily. This was the most pronounced bacteriostatic effect in the series, but the recurrence of the pathogen after the fifth day coincided with diarrhea of a more serious nature than that of the initial infection. A possible explanation is the recurrence of the infecting organism in the gastro intestinal tract at a time when the normal flora had not yet returned, allowing for a more rapid growth of the pathogen, and an increased toxic action.

The clinical effect of the therapy in these five cases cannot be judged conclusively. The general symptoms were mild and did not differ materially from those in the control cases. No systemic generalization of the infection took place.

In animals, the clinical effect consisted only of the postponement of the final, often fatal, outcome. In human beings, with a generally milder infection, this delay of pathogenic action may have therapeutic value. The action of streptomycin might secure a safety zone until the patient is able to build up his own biologic defense. Prolonged treatment would probably suppress toxic action at least temporarily and thereby spare infants added hazards in the most labile time of their life. This, of course, is mere conjecture; but it gives the warrant for further therapeutic studies in this field.

SUMMARY

1. Five infants infected with *S. typhimurium*, were treated with streptomycin; four of them by oral administration only, one with combined oral and parenteral therapy.

2. The clinical course of the infection was rather mild in the treated and untreated infants. The effect on the symptoms of the disease could not be appraised.

3. Doses from 25 to 100 mg. orally given at intervals of three hours succeeded in suppressing the growth of the normal fecal bacteria as well as the pathogenic organism.

4. Discontinuance of treatment resulted in quick reappearance of *S. typhimurium* and the normal fecal flora.

5. Salmonella organisms isolated after the end of treatment showed no increased streptomycin resistance.

6. Almost identical results were obtained in animal experiments.

7. The possible therapeutic value of the limited bacteriostatic effect of streptomycin in salmonellosis is discussed.

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DEVELOPMENTAL PEDIATRICS

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PEDIATRICS is unique among the specialties of clinical medicine. Other specialties are focused upon a single organ system or some one aspect of the human organism, while pediatrics is focused upon the early sectors of the life cycle and remains a form of general medicine concerned with the total child. It derives its strength and also a distinctive social significance from this kind of specialization.

Whatever social legislation the future may hold, the inherent technologic trends in medicine will lead to a mobilization of diagnostic and supervisory resources at the beginnings of the life cycle. By necessity as well as by tradition, pediatrics holds the most strategic position in the whole scheme of preventive and constructive medicine, since health protection begins with the beginning of life and growth.

The first task is to insure survival of the newborn infant. The second task is to safeguard his optimal growth. By this simple logic, development as well as disease falls within the province of clinical pediatrics. The present paper attempts to indicate how the diagnosis and supervision of infant development may be more fully incorporated into the arrangements of pediatric medicine, both at the level of the practitioner and at hospital and health centers.

THE CONCEPT OF DEVELOPMENT

The concepts of development and disease cannot, of course, be divorced. In many diseases it is the developmental consequences which are of critical concern. The severity and the incidence of disease are influenced by age and maturity. The vast field of allergy and immunity involves developmental factors at every turn. Many abnormal and atypical modes of development must be interpreted in terms of disease. In cases of blindness and deafness and of sensorimotor impairment, the effects upon the course of development are of supreme importance. Even malnutrition may lead to maldevelopment. Indeed, health may be here defined as that optimal condition of a growing organism which denotes and fosters a maximum of development.

For such reasons, the practitioner never escapes problems of development, whether he is "merely" supervising the nutrition of a well baby or following the growth career of a chronically sick, handicapped, or defective child. All children, normal or abnormal, are confronted by the universal problem of growing up, and the parents who make up our society are looking first of all to medical science for help in the complex task of rearing their children.

To be sure, there are many parents who are overanxious, and who, in a shallow, emotional way, are overconcerned about the psychology of their young offspring. They think in terms of conditioned reflexes and subconscious complexes, and they use foreboding psychoanalytic phrases to give voice to their

worries and misinterpretations. There is a good deal of sophisticated superstition due to misleading popular education. The widespread breakdown of wholesome family life has added to confusion and insecurity. This simply heightens the significance and the responsibilities of sane pediatric medicine. Without adequate medical safeguards for child hygiene, we may anticipate an increase in the influence of unscientific cults and of superficial forms of psychologic counseling, mental testing, and personality guidance. The protection of the mental health of the oncoming generation should be based upon an individualized medical protection of infants and children. Developmental pediatrics is a form of clinical medicine which is especially concerned with the diagnosis and supervision of child development.

The mounting emphasis on mental health is in part due to the stress and hardship of the troubled times in which we live, and into which babies are being thrust. But the emphasis is also a natural outcome of the progress of medical knowledge.

Biologic and clinical science has demonstrated the intimate relationship of structure and function to such a degree that the old antitheses of mind versus body, heredity versus environment, and psyche versus soma have lost much of their force. The organism is regarded as an indivisible unit in which physical well-being and mental welfare are reciprocal and inseparable. This monistic outlook has such far-reaching implications for medicine, that it has recently taken on the formidable, hyphenated designation, psycho-somatics. In fact, if we drop the hyphen, the union of psyche and soma becomes complete!

Psychosomatic medicine is nothing new. It simply represents a more incisive recognition of the interaction and basic identity of physical and functional factors. Development, likewise, is a unifying concept which acknowledges that the laws and mechanisms of growth apply equally to body and mind. The infant comes by his mind (psyche) in the same embryologic way that he comes by his body (soma).

DEVELOPMENT AS A CLINICAL PROBLEM

But development is a living process, as well as a philosophical concept—a process as real as respiration or metabolism. The nature of this process is being investigated by a great variety of ingenious methods, both in lower and higher organisms. Growth, in all its aspects, normal and abnormal, has become the central problem of the biologic sciences. It is now apparent that the growth of tissues, organs, and behavior is obedient to universal laws of developmental morphology. These laws make for a certain degree of predictability of growth phenomena. As our knowledge of these laws deepens, human growth will come increasingly within the scope of clinical diagnosis and medical control.

All this rapidly evolving science is destined to make itself felt in the procedures of clinical pediatrics. In health and in disease the child will be more and more appraised in terms of growth characteristics and of developmental status. (We use the words *growth* and *development* interchangeably.)

INDICES OF DEVELOPMENT

Developmental status manifests itself in three major kinds of signs and symptoms: anatomic, physiologic, and behavioral. All of these manifestations

are important from the standpoint of a developmentally oriented pediatrics.

Anatomic indices become significant when they go beyond mere height and weight, and deal with girths, body proportions, somatotypes, and growth rates. The new interest in the physical anthropology of the child will probably lead to rapid photographic, and other methods of recording, which sum up valuable data pertaining to constitutional type.

Physiologic indicators can furnish much evidence concerning growth conditions because the bodily states of the organism change with age. With the remarkable advances now under way in biochemistry, electrometry, and micro-measurements, the physiologic diagnosis of infant development may in time reach a high degree of refinement and accuracy.

Behavior, however, will always remain the most comprehensive and the most sensitive indicator of developmental status. Medically considered, the infant is an action system which reveals itself in patterns of behavior. His behavior characteristics and capacities infallibly express the maturity of his neuromotor equipment and the achieved efficiency of his total organism.

The developmental diagnosis of infant behavior, accordingly, constitutes the major task of a developmental pediatrics. Anatomic and physiologic criteria of growth and well-being can never be safely ignored or slighted; but they must always be correlated with the crucial criterion of behavior. The motor, the adaptive, the language, and the personal-social behavior of the child sums up most completely his capacity to grow.

To appraise his behavior we need systematic methods of interview, observation, and diagnosis. To elicit significant behavior patterns we must use standard techniques skilfully adapted to individual and age differences. The examination must be conducted formally, with precision of purpose. In some twenty minutes we aim to have the infant display his most characteristic responses: his postural adjustments, his oculomotor control, his visual and auditory perceptiveness, his coordination of eyes and hands, his prehension, manipulation, and exploitiveness; his social awareness and communicativeness; the range and patterns of his attention, his general adaptivity, alertness, and competence to meet the total sequence of the examination. An amazingly rich array of significant behavior patterns can be evoked by a standardized sequence which uses the plain appurtenances of a crib, a table surface, and a series of simple test-objects.

THE FUNCTIONS OF DEVELOPMENTAL DIAGNOSIS

In the hands of a clinician, who can bring a background of experience to bear upon his findings, a developmental examination of behavior serves at least five functions:

1. It ascertains the stages and patterns of developmental maturity in normal, subnormal, and superior infants.
2. It analyzes the total behavior equipment into components and makes possible differential diagnoses of normality, amentia, and specific developmental deviations.

3. It brings to light neurological defects and sensory impairments not disclosed by ordinary methods of clinical examination. (It is indispensable for detecting many mild and obscure forms of cerebral injury.)
4. It supplies important objective information concerning emotional traits and the organization of personality.
5. It implements a constructive type of developmental supervision. Periodic developmental examinations define the growth pattern peculiar to the individual child and become the basis of a consecutive individualized child and parent guidance.

MEDICAL EDUCATION FOR DEVELOPMENTAL PEDIATRICS

When the functions of developmental pediatrics are stated in the foregoing terms, it is clear that a more fundamental training of physicians in this field of medicine is indicated. This training should begin in the undergraduate years and may be carried through to a high level of postgraduate specialization. The medical student in his preclinical and clinical years should have more systematic instruction in the physical and physiologic aspects of child development. This need not entail a multiplication of independent courses. On the contrary, an adaptable educational program would correlate an increasing amount of teaching and demonstration about a few key subjects such as growth and development.

The student of pediatrics, in particular, should be infused with the doctrine of development, because this alone can give him adequate perspective for appraising the normal and abnormal symptomatologies of infancy. By systematic consideration of the somatic, physiologic, and behavioral manifestations of development, it will be possible to raise the study of normality to the dignity of a clinical subject. Clinical and supervisory pediatrics is preeminently concerned with the protection and the augmentation of normal well-being. For this reason it is anomalous that the critical diagnosis and interpretation of normal child development has such meager status in medical education.

Training at a postgraduate level should be associated with interneships and residencies. This will become possible only when hospitals and teaching centers recognize the field of developmental pediatrics as a subspecialty which must have distinctive facilities in the form of a separate locus, appropriate equipment, and expert personnel on a par with other diagnostic subdivisions.

A well-grounded pediatrician can be trained to expertness in one or two years of full-time participation in a diagnostic and advisory service which deals with a wide range of normal and abnormal developmental conditions. Ideally, this specialized training should include the periodic contacts of well-baby supervision, the examination of infants prior to adoption and foster home placement and of preschool children under nursery school auspices, and the differential diagnosis of a diverse array of mild and severe abnormalities, including retardation, amentias, aplasias, malformations, degenerative processes, cerebral injuries and other traumas, anoxemia, infections and toxic lesions, endocrine dysfunctions, sensorimotor handicaps, and environmental shocks and stresses.

DEVELOPMENTAL PEDIATRICS AND PSYCHIATRY

The mere enumeration of all these conditions reminds us how gravely they may be neglected in the absence of facilities for developmental diagnosis and supervision. In virtually every instance, whether the child be normal, handicapped, or defective, the crucial medical and social problems call for a judgment as to developmental status, developmental outlook, developmental guidance. And since these problems all gravitate in their first, infant phase to the pediatrician and the family doctor, the primary responsibility for their solution gravitates to the pediatric contingent of the medical profession.

We know of no other specialty equipped to take over this inevitable task of preventive and supervisory medicine. Allergist, cardiologist, orthopedist, neurologist, and psychiatrist all have a role to play; but the pediatrician alone is conversant with the infant as a whole, and he is preeminently concerned with the maintenance of a forward moving sequence of development. The pediatrician is adept with babies, and by tradition he is interested in their total welfare. So he is in a favorable position to go along with the new trends of psychosomatic medicine, and with the new scientific emphasis on the dynamics of development.

The historical evolution of clinical pediatrics has very naturally brought about a preventive outlook upon the period of infancy and early childhood. Psychiatry, on the other hand, has derived its concepts largely from the psychopathology of the adult, and has been preoccupied with the interpretation and treatment of mental disease. Recent extensions into the adolescent and preadolescent period therefore reflect the methods and the outlook of adult psychiatry. Accordingly, child psychiatry has made its most characteristic contribution in psychotherapy, and in the elucidation of the abnormal behavior which manifests itself in juvenile conflicts with adult culture.

Experts in the field of abnormal child behavior will always be in strong demand to serve as consultants or as members of a diagnostic group. In view of the historical trends of psychiatric medicine, this represents a logical function of a clinical child psychiatry.

For the vast work of preventive mental hygiene, however, we must look to pediatric medicine. In principle and in actuality, pediatrics is already committed to a form of supervisory health protection which includes mental as well as physical welfare. Since bodily growth and psychic development cannot be divorced, the methods of developmental pediatrics contain the essence of a preventive psychiatry of infancy and childhood.

To understand any child, whether normal or handicapped, we must understand his ways of growth. These ways of growth are the sum and substance of his psychic constitution, or his psychosomatic constitution. Only as we become aware of these ways of growth, can we plan adequate procedures of guidance and control. Here lies the significance of a periodic examination of infant behavior as a pediatric approach to the mental hygiene of early child development.

AREAS OF APPLICATION

A brief outline of the possible areas of application will serve to summarize the main thesis of this paper.

Developmental pediatrics is a special form of clinical procedure designed for the diagnosis and supervision of early child development.

It is equally concerned with normal and abnormal development because its aims are preventive, positive, and directive.

The scientific foundations and techniques of developmental diagnosis are now in the making. The American Board of Pediatrics has recognized the new trends by a pioneering policy which has made knowledge of growth and development a prerequisite for specialty certification.

This knowledge should embrace the behavioral as well as the somatic and physiologic aspects of child development. Behavior is the most inclusive and significant index of developmental status and is the most essential clue to the developmental needs of infant and child.

Periodic determinations of developmental status serve to protect the mental health both of normal and of handicapped children.

For reasons of social welfare, such developmental supervision is of preeminent importance during the first three or five years of life.

For concreteness, several areas and degrees of application of developmental pediatrics may be outlined as follows:

General Pediatric Practice.—The busy practitioner who has little time for extras of any kind should nevertheless consider the value of a routine behavior inventory. This inventory would be a check list of behavior items ascertained by questioning, directed observation, and a few simple tests. A minimum of eight items covering the motor, language, adaptive, and personal-social reactions of the child could be used to screen significant defects and deviations. In conjunction with the physical record such items may at times assume much importance in the later developmental history of the child.

Dispensaries, Children's Wards, and Temporary Homes.—A routine behavior inventory can serve a similar screening purpose where numbers are large and personnel is limited.

Child Care Institutions and Agencies.—Here child protection should go one step beyond physical health. More careful appraisals of developmental status should be made from time to time. Even if nurses, social workers, and psychologists assist in making the records, the responsibility of interpretive diagnosis should remain with the supervising physician. Infants and young children should not be placed in adoption without a thorough developmental examination, followed by a period of probation.

Individualized Pediatric Supervision.—Pediatricians with requisite skill and aptitude can incorporate varying degrees of formal developmental work into their regular nutrition and health supervision. Much can be done, much is being done, by way of developmental guidance, in a purely incidental manner. Much more could be done if this guidance were specifically related to a

series of planned examinations at key ages. Consecutive appraisals with standardized procedures would lead to more insight into the individuality of the child's growth pattern as expressed in his modes of development.

The same kind of supervision would be highly desirable in well-baby conferences. There is a growing realization that the methods of these conferences should be more thoroughgoing, which is to say that they should be more individualized and focus more fully on developmental factors.

Medical Teaching Centers and Regional Hospitals.—Here the need of a highly specialized form of developmental pediatrics is now unmistakable. To the large hospitals, research and teaching centers come an unending stream of infants and young children who present developmental complications of far-reaching and long-enduring import. Too often these young patients receive only a delimited categorical diagnosis which overlooks or slights the developmental essence of their condition. But it is the developmental aspect which is of supreme concern to the parents. The medical management of these cases of abnormality, impairment, and handicap, becomes more considerate with a developmental approach, which leads to constructive follow-up contacts during the trying early years when parents profit most from timely and skilful guidance. Incidentally, a careful developmental examination which parents are permitted to observe often helps them to better understand their child and the methods of care which he will need at their hands.

The first and foremost function of developmental pediatrics in a large clinical center is diagnosis; because diagnosis involves a concrete estimate of growth potentialities and thereby serves to define the details of care and management. Diagnosis becomes cumulative and progressive with follow-up contacts. In developmental supervision, interpretive diagnosis and advisory guidance are closely combined in the interest of child and parent.

The recognition and interpretation of developmental defects and deviations, however, requires a vivid acquaintance with the characteristics of normality. The clinician will, therefore, see to it that he and his students make ample contact with relatively normal infants and children at varying age levels. Provisions for the developmental supervision of "normal" infants may some day become an accepted feature of hospitals which also function as health centers. Certainly the public health activities of the future will become increasingly clinical; that is, individualized, and they will place a prior premium on mental health in infancy and preschool childhood.

In view of the great dearth of experienced developmental pediatricians, we shall have to look to medical schools and teaching centers for the training of specialists in this most generalized form of clinical medicine. The larger institutions can well set aside a special locus, with simple but hospitable arrangements designed for the conduct of systematic, formalized, developmental examinations. These arrangements would be available to normal infants under health supervision, as well as to the deviant and defective. When such provisions are deliberately planned and utilized by expert clinicians, developmental pediatrics will come into its own both routinely and as a diagnostic specialty.

TETANUS

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DURING the years 1921 to 1946 there have been seventy patients with tetanus admitted to the wards of the Hospital for Sick Children, Toronto. It is the purpose of this report to present some observations on this disease with special reference to improvement in methods of treatment.

CLINICAL ASPECTS

We have had an opportunity to study the value of administering antitoxin by different routes. Usually, the source of the infection in these patients could be traced to a scratch, a cut, or a punctured wound. In fifteen of the seventy patients, no history of injury was obtained. There was a great variation in the clinical course from very severe to very mild cases. Incubation periods varied from one day to one month, and usually, the shorter the period, the more seriously ill was the patient. Although the prognosis was definitely less favorable in patients with a short incubation period, the invasion period was of more importance in determining the prognosis; the more rapid the invasion period, the more likely the patient was to succumb.

It was found that most of the cases occurred during July, August, and September, and that the majority of the patients ranged in age from 3 to 13 years. Two were in the neonatal period. Fifty-three were boys and seventeen were girls.

TREATMENT

The patients are kept in a quiet, darkened room with nurses in constant attendance. Fluids by mouth are given as long as possible if they do not cause spasms and choking. Intravenous fluids are given when oral feedings are no longer possible. Antitoxin is administered intramuscularly in doses of from 40,000 to 300,000 units in the course of the first few days after admission, the dosage depending upon the severity of the signs (i.e., degree and frequency of spasm). If a respiratory infection develops during the course of treatment, penicillin is administered. Seconal, as suggested by Dietrich,[11] has been used almost exclusively in doses of ¾ to 3 grains depending on the age of the patient and the severity of the spasms. Wounds have not been excised in recent years, as some patients were worse after this procedure. The wound, however, should be cleansed by the usual conservative methods.

RESULTS

The results are shown in Chart 1. The fatality rate from 1921 to August, 1946, was 47 per cent. This rate takes into consideration all patients with tetanus, including three patients who died before treatment could be instigated,

From the Department of Pediatrics, University of Toronto, and the Hospital for Sick Children, under the direction of Alan Brown, M.D., F.R.C.P. (London).

and one patient, the history of whom showed no record of the amount of antitoxin, although we believe antitoxin had been given. During the years 1921 to 1928, there was a patient fatality rate of 66.6 per cent, during 1929 to 1935 the rate was 55.5 per cent, and from 1936 to August, 1946, it had fallen to 28 per cent. We believe that these results over a twenty-five-year period reveal that our treatment has improved in respect of the route of administration of antitoxin. We believe that there are other factors as well which explain this result; namely, continuous nursing, more careful feeding of the patients, the use of seconal as a sedative, and the observation that many patients in recent years have had a less severe type of illness.

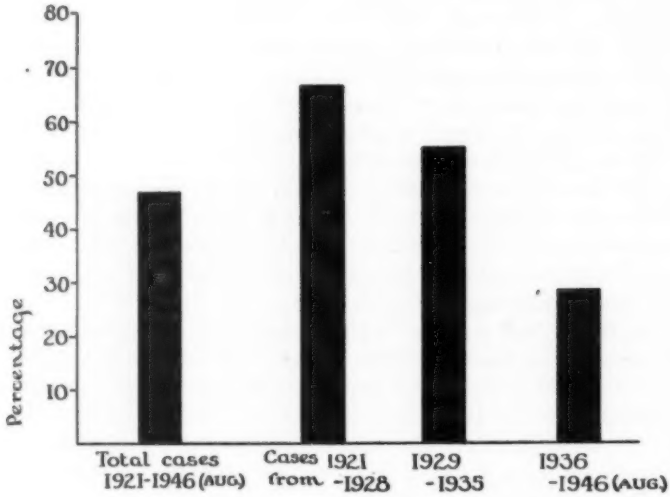

Chart 1.—Tetanus fatality rate in per cent for seventy cases from 1921 to August, 1946.

DISCUSSION

Due to the fact that fifteen of our seventy patients had no history of injury, that repeated doses of antitoxin sensitize children to horse serum, and that many children are allergic, we believe that consideration of the prevention of this disease in all children is paramount.

The prevention of tetanus with tetanus toxoid should be practiced in conjunction with administration of diphtheria toxoid and whooping cough vaccine.

In evaluating the treatment of our patients, we believe it is worth-while to discuss some of the more important observations. In the period from 1929 to 1935, the majority of patients received large, intravenous doses of antitoxin. A few of these patients developed reactions soon after intravenous therapy which suggested anaphylactic shock. We felt at times that this produced a pulmonary edema which could have resulted from antitoxin and fluids intravenously in the presence of heavy sedation. We believe that intrathecal administration of antitoxin is unsound and probably dangerous. This method of

administration of serum produces a sterile meningitis which adds to the patient's discomfort and may decrease his chances of recovery. In the past few years, 1940 to August, 1946, fifteen patients received tetanus antitoxin by the intramuscular route exclusively. In addition, most of them received seconal as the sedative. We believe that this method of administration of antitoxin is to be preferred to either the intravenous or intrathecal routes and should be used exclusively. In a review of these patients it will be seen in Chart II that methods of treatment formerly used, in which antitoxin was given by various routes or combinations of routes, resulted in as many deaths as recoveries. In the group of fifteen patients to which intramuscular injections of antitoxin were given, there were only two deaths and thirteen recoveries.

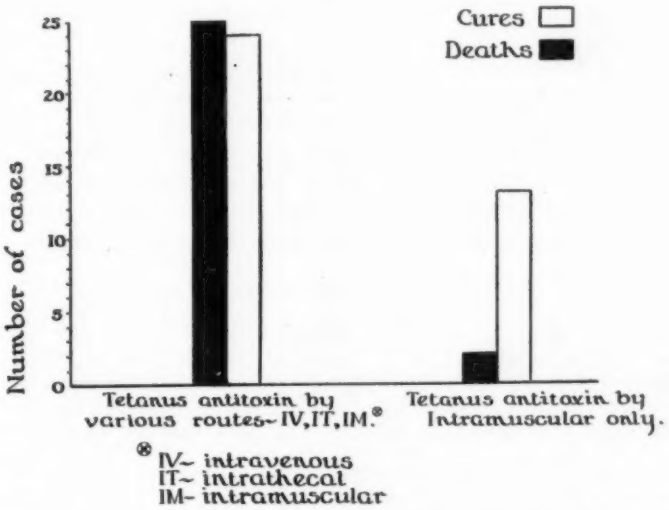

Chart 2.—Tetanus antitoxin in treatment of sixty-four patients from 1921 to August, 1946.

It may be well at this stage to discuss the measurement of the blood antitoxic unit before and following therapeutic doses of tetanus antitoxin. This was done in a few of our patients. It is known that a dose of tetanus antitoxin of therapeutic proportions elevates the blood antitoxin to levels which have been assumed to be sufficient to neutralize disseminating toxin. This is rational in theory; yet in practice we have observed patients, who received amounts of antitoxin resulting in satisfactory blood levels, improve during the days in which antitoxin was given; later, these patients developed more frequent spasms, were then given more antitoxin as well as continued sedation, and have shown definite clinical improvement. It may be argued that it was not the additional antitoxin that had the desirable effect, yet after noticing the improvement in certain patients over some years past, we believe that additional amounts of antitoxin are beneficial.

SUMMARY

1. Seventy cases of tetanus are reported.

2. In fifteen patients there was no history of injury.

3. The incubation period, invasion period, the seasonal, age, and sex incidence of these cases are mentioned.

4. Active immunization as a means of preventing tetanus is discussed and recommended for all children.

5. In treatment, tetanus antitoxin is recommended in doses of 40,000 to 300,000 units, to be given intramuscularly.

6. We do not recommend that antitoxin be given either intravenously or intrathecally.

7. Seconal is the sedative of choice.

8. Nurses should be in constant attendance and the patient kept in a quiet, darkened room.

9. Surgical excision of the focus in the early acute stage of the disease is not recommended. The wound may be treated conservatively by the removal of easily accessible splinters or other objects, properly cleaned, and protected.

10. Results of treatment in the period from 1921 to August, 1946, show that in the seventy patients there was an overall fatality rate of 47 per cent. From 1921 to 1928 the fatality rate was 66.6 per cent, from 1929 to 1935 it was 55.5 per cent; and from 1936 to August, 1946, it was 28.5 per cent.

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Case Reports

REPORT ON A PREMATURE INFANT WEIGHING 820 GRAMS

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THE number of premature infants weighing less than 900 Gm. and surviving is small, so that a case of this sort is of interest. The smallest infant reported was by Fischer-Ban,[1] weight, 600 Gm. The smallest infant reported in this country was by Hoffman,[2] weight, 735 Gm. at birth. Dr. Julius H. Hess[3] stated, "The child mortality after cesarean section was strikingly high (45 per cent), which, however, was not due to the operation but to complications on the part of the mother, namely, eclampsia and placenta previa." In our case the infant was not only premature (twenty-seven weeks' gestation) but was delivered by section because of eclampsia and premature separation of the placenta.

The mother of this infant was a white woman, aged 33, with a history of one previous abortion. Her last period had been Jan. 24, 1943. On August 13 she came into the hospital with severe symptoms of toxemia, semicomatose, blood pressure 220/110, and vaginal bleeding. After eighteen hours of treatment with intravenous fluids, morphine, a cesarean section was performed by Dr. A. F. Lash, and a female fetus delivered. There was a large retroplacental hematoma.

The infant at birth was cyanotic, showed no muscular activity, no cry, and very feeble respiratory movements. Immediately after birth the mouth was cleared with a catheter, and the infant placed into an oxygen incubator of the Hess type which had already been made ready in the premature nursery. An ampule of Vitamin K was given and repeated every six hours for 4 doses. The weight a few hours after birth was 820 Gm., and length 30 centimeter.

Nothing was given by mouth for twelve hours, then sterile water about 5 drops every two hours for twelve hours, then breast milk diluted one-half with saline for forty-eight hours, then full strength breast milk. After eight days she was taking 4 to 6 c.c. every two hours. On the fifth day the first audible cry was heard. The incubator temperature was kept at 90° F. up to the ninth day, when the baby began to run a slight temperature; after this it was lowered to 84° F. From then on, no temperature difficulties were encountered except on the eighteenth day when the incubator was accidentally heated to 100° F. and the baby's temperature went to 103° F. No ill effects were noted.

The weight, which started at 820 Gm., was 893 Gm. on the twelfth day (no intermediate weighing was done). On the twenty-third day the infant weighed 1,015 Gm.; on the twenty-ninth day, 1,090 Gm.; on the thirty-fourth day, 1,175 Gm.; on the forty-second day, 1,309 Gm.; on the forty-fourth day, 1,300 Gm.; on the forty-sixth day, 1,390 Gm.; on the fifty-fourth day, 1,514 Gm.; on the sixty-first day, 1,816 Gm.; and on the seventy-eighth day, 2,327 grams. On leaving the hospital on the eighty-fifth day, she weighed 2,549 grams. Cyanosis and irregular respiration were present up to the fifth day, after which very little respiratory difficulty was encountered. Oxygen was continuous, however, up to the twenty-sixth day, and intermittent (after feedings) up to the forty-fourth day. Feedings were by dropper up to the twenty-fourth day, by the premature nursery bottle up to the thirty-fifth day (1,175 Gm.), then by ordinary bottle. No regurgitation was encountered except when the feedings were pushed faster, or more than the baby wanted.

Straight breast milk was given from the third to the fifty-fifth day (supplied by the Chicago Board of Health), then a gradual shift to lactic acid milk was begun. The lactic acid milk had to be given double strength to maintain weight gain. In addition, Vitamin B complex, and orange juice were started on the twenty-fourth day, oleum percomorphum on the twenty-ninth day, and iron and ammonium citrate, a 50 per cent solution, 5 drops in each bottle, on the fifth day.

Father's blood, 2 c.c., diluted with 2 c.c. of saline was given at six hours, at twenty-four hours, and then every other day for three weeks, then every five days until discharge, the amount being gradually increased.

On October 4 (forty-eighth day), the blood count was: red blood cells, 3,700,000; white blood cells, 10,200; hemoglobin 12.1 Gm.; 15 per cent segmented cells; 3 eosinophiles, 1 basophile, 71 small lymphocytes, and 10 monocytes. On October 19 (just before iron was started), the count was: red blood cells, 3,100,000; white blood cells, 10,100; hemoglobin, 11.0 Gm.; segmented cells 18%; eosinophiles 6; small lymphocytes 69; monocytes 6; and 1 Türk cell.

Further feedings consisted of cereal begun at 45 days, vegetables at 4 months, and the usual form of feeding from then on. At 3 months, the milk was changed to evaporated milk, water and dextri-maltose, and at 9 months to cow's milk.

At one year the baby weighed 15 pounds, 9 ounces, was 23 inches long, crawled, and had four teeth. Though small, she acted like a normal infant of her age. At 2 years she weighed 24 pounds, was 29 inches tall, walked and ran normally, and spoke short sentences. At 3 years she weighs 30 pounds, is 35 inches tall, walks, runs, talks well, and seems quite bright for her age. At 18 months she had bronchopneumonia, at 26 months measles, and several attacks of tonsillitis at various times. With each illness, she ran a temperature of 104° F. or over, but recovered quickly with no ill effects.

I believe part of our success in this case was due to a minimum of manipulation at birth, and careful, patient management on the nurses part in the early stages.

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INFANTILE TOXOPLASMOSIS

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REPORTS of human toxoplasmosis have been increasingly frequent in the past few years. Among various factors which have contributed to this increased incidence are more accurate knowledge of the history and morphology of the toxoplasma organisms and their demonstration within the monocytic phagocytes of the body, the development of neutralization antibody and complement fixation tests, the transmission of the condition to experimental animals by infected body fluids or tissues, and a better appreciation of the various clinical aspects of the disease.

The progress which has been made in diagnosis is indicated by the recognition of four fairly distinct clinical types,[1, 2] each with characteristic signs and symptoms. These may be briefly outlined as follows: (1) the congenital or infantile type with the infection occurring either in utero or shortly after birth and giving signs of cerebral injury, such as convulsions, hydrocephalus, microcephalus, mental retardation, chorioretinitis, or calcification of the irregularly distributed granulomata which have occurred within the central nervous system, (2) an acquired disease in older children characterized by acute encephalitis, (3) an acute form in adults with pneumonia, and at times, a picture resembling typhus or spotted fever, and (4) a group in which high natural resistance to the organism has resulted in the production of neutralization antibodies[3, 4] in the serum with an absence of any clinical signs attributable to the toxoplasmic infection. The case to be reported belongs to the first classification and an early tentative diagnosis of toxoplasmosis was made because of the presence of disseminated, calcified areas in roentgenograms of the skull.

The first published record of proved human toxoplasmosis was in 1939 by Wolf and associates,[5] in a child from whom the infection was experimentally transmitted to laboratory animals. These authors also included in this report four additional cases previously described by other investigators[6, 17-19] as due to an Encephalitozoon, and which Wolf and his associates now believe to be toxoplasmosis. These same authors[8] in 1942 reported six other individuals diagnosed clinically. Three of these six patients had been mentioned in a review in 1941 by Sabin,[3] who collected all of the proved and probable toxoplasmic infections to that date. This review summarized seventeen cases, including twelve of the infantile type, two of the acquired childhood, and three of the adult type. Four of the children were alive at the time of writing.

In 1940 Pinkerton and Weinman[7] described the first recognized infection in an adult. Other cases, most of which have been children, have been reported by Pinkerton and Henderson,[10] Levin and Moore,[11] Vail and associates,[12] Crothers,[13] Adams and associates,[14] Steiner and Kaump,[15] Tomlinson,[16] and Syverton and Slavin.[2]

Zuelzer,[1] in 1944, reported infantile toxoplasmosis in three children, two of them being identical twins.

In 1946, Pratt-Thomas and associates[9] summarized twenty-one deaths due to this disease, with necropsy reports. At the present time, so far as I have been able to ascertain, a total of thirty-eight cases have been reported.

From the Children's Hospital of Pittsburgh.

CASE REPORT

C. K., a 4-year, 3-month-old, white female, was first seen on May 23, 1946, in the outpatient department of the Children's Hospital of Pittsburgh, where she was brought because of intermittent convulsions which had begun at the age of 2½ months. During the course of preliminary study, routine skull plates showed multiple intracranial calcifications, which were recognized in the x-ray department as possibly indicating infantile toxoplasmosis. The child was admitted to the hospital on June 11, 1946, for further study.

History.—With the exception of a lethargy lasting a few hours after birth, the baby was normal until 2½ months of age when she had a severe bout of diarrhea lasting a week. During this period of illness she had many convulsions of several minutes' duration. At 2½ years, she began to have a right-sided convulsive seizure resembling petit mal, which disappeared for fifteen months on treatment by the family doctor. About six months previous to admittance to the hospital the attacks recurred and were as frequent as five or six times a day, usually in the morning. Her eyes wavered from side to side, her head dropped for a few seconds, but there were no definite convulsive movements. She was drowsy following these attacks. The child had had no illness other than German measles in April, 1946, frequent colds, and an occasional attack of tonsillitis.

The mother had been comparatively well during pregnancy, her only complaint being that she had severe hemorrhoids. The pregnancy was of eight months' duration. Birth weight was 5½ pounds. The child cut her first tooth at 13 months and at the time of writing had twenty teeth. She sat up at 8 months and walked at the age of 2 years. At the present time she says words but does not form them into sentences. Both mother and father were living and well. The family had always lived around Pittsburgh except for the mother, who lived in New York City from 1931 to 1936. The mother had never had any illness except the usual contagious diseases and her pregnancies. There was one other child in the family, a boy aged 7 years, in perfect health. The mother had no other miscarriages and no other pregnancies. There was no history of familial diseases. The parents offered the information that at the time of birth of this child the mother was told that she had a positive Wassermann test. This was disproved at subsequent blood tests done in this city.

Physical Examination.—The patient was a white female child of 4 years, 3 months, fairly well developed, but definitely mentally retarded. Her weight was 33½ pounds, height, 38 inches. The head circumference was 46.35 cm. (normal, 49 cm.). There were no skull deformities. The other positive physical findings were a lateral nystagmus of both eyes. Ophthalmoscopic examination showed several large areas of chorioretinitis in the right eye. The left eye had one large area of chorioretinitis in the lower quadrant. There was a suggestion of a positive Bakinski test in the left foot. Other reflexes were normal.

Laboratory Data.—Hemoglobin was 12.5 Gm.; red blood cells, 4,240,000; white blood cells, 7,400; polymorphonuclears, 75 per cent; lymphocytes, 13 per cent; monocytes, 1 per cent; eosinophiles, 5 per cent; myelocytes, 6 per cent. Blood calcium was 9 mg. per cent; blood phosphorus, 5.4 mg. per cent; and blood phosphatase, 10.24 Bodansky units. The urine was negative except for an occasional pus cell and some mucous shreds, and the blood Kahn test was negative. Old tuberculin tests were negative 1:10,000 and 1:1,000; the sedimentation rate was 22 mm. per hour. Spinal fluid examination showed the pressure to be within normal limits; the fluid was clear; the cell count

was 1 lymphocyte; globulin was negative; the smear was negative and culture showed no growth. Spinal fluid sugar was 63 mg. per cent; chlorides, 715 mg. per cent; and proteins, 54.5 mg. per cent.

X-Ray Report.—There was a large number of small, calcified particles scattered throughout the brain. These probably represent calcifications accompanying infestation with toxoplasma (Fig. 1).

The chest, pelvis, long bones, and abdomen were entirely negative to x-ray examination.

Psychometric Examination.—The patient cooperated well. Her I.Q. was 65 with a mental age of 34 months. "The patient demonstrated an ability to learn. Therefore, another test in six months or a year would be indicated. She compensated for lack of speech by very meaningful gestures."

Neutralization Antibody Test.—On July 19, 1946, blood was taken from the patient and from the mother for neutralization antibody tests. It was centrifuged and packed in dry ice and sent to Dr. Isaac Ruchman at the Children's Research Foundation in Cincinnati. Dr. Ruchman reported positive neutralization tests for both the patient and the mother.

Ophthalmoscopic examinations were done on the mother, father, and other sibling, all of which were normal. X-rays were also done of the skulls of the mother, father, and other sibling. These were also negative. The brother of the patient was a 7-year-old boy, very healthy in appearance and well developed. He gave no history of any illness in the seven years of his life.

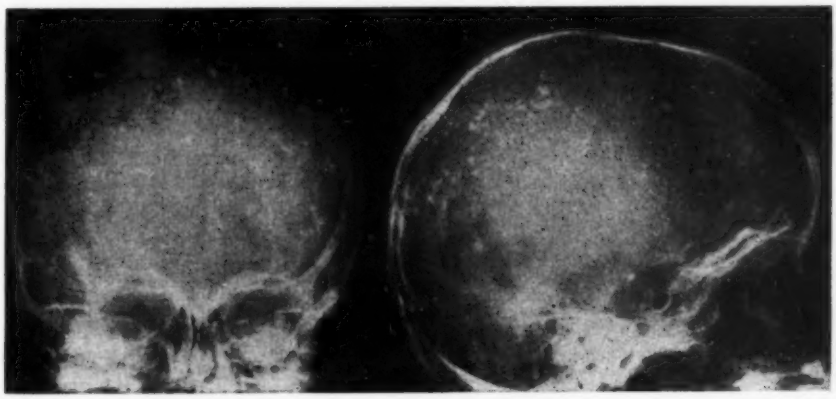

Fig. 1.—Toxoplasmic intracranial calcifications.

DISCUSSION

This case represents a typical picture of congenital or infantile toxoplasmosis, similar to the cases reported by Wolf and associates[8] in 1942. The fact that the mother showed neutralization antibodies in her serum would make it seem likely that the child had acquired the disease in utero. However, it cannot definitely be proved that the diarrheal episode, which occurred at the age of 2½ months, was not the onset of the infection. The head circumference was slightly below normal, but was not definitely microcephalic. The intracerebral calcifications were extremely numerous and certainly would account for the degree of mental deficiency. Toxoplasma were not found in the spinal fluid, probably due to the long duration of the infection. Tissue biopsies were not done, and so the organism was not isolated, but certainly the clinical picture and the positive neutralization antibody tests were enough to classify

this case as one of infantile or congenital toxoplasmosis. Unfortunately, blood was not taken from the father or the other sibling, and so we do not know if either or both of them might have showed a clinically inapparent infection.

SUMMARY

1. A case of congenital or infantile toxoplasmosis is presented.

2. The infection was probably acquired in utero, suggested by the positive neutralization antibody tests on the mother.

3. This child represents clinically another typical case of infantile toxoplasmosis that has survived.

I wish to express my appreciation to Dr. Isaac Ruchman of the Children's Research Foundation in Cincinnati, for his work on the neutralization antibody tests on this case, and to Dr. Maud L. Menten, Pathologist, Children's Hospital of Pittsburgh, for her assistance in organizing the material presented.

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Special Article

THE NURSE AND THE CHILD IN GREEK LIFE

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SOCIAL STATUS OF THE NURSE

THE helpless condition of infancy has always called for special offices to tide the child over the first years of life. These are performed either by mother or nurse. Among the Greeks, the nurse is a familiar figure in the household, and although our knowledge of Greek domestic life must necessarily be limited from the fact that the women's apartments are so persistently closed against us, nevertheless, from sidelights furnished by our threefold source of information, the literature, the arts, and the inscriptions, we cannot help being impressed by the important place which the nurse held in the family.

In the Homeric age, mothers nursed their own children. Still, there are some instances pointing to a different practice. Odysseus, in addressing his old nurse, Eurycleia, says, "It was thou that didst nurse me here at thy own breast."[1] Nurses were employed as the attendants of the children, whom they amused and brought up as long as they remained in the house of the parents. Whatever function she performed, the Homeric nurse was a slave, either a captive[2] or purchased as an ordinary slave.[3] The Phrygian nurse of Hector's son may be taken as the model of the Greek nurse of an infant. We infer from her occupation that she was a slave.[4] Eumaeus' nurse gives us an instance of the nurse of an older child.. She had been captured and sold as a slave to her master, whose hard bond she feared.[5] Eurycleia was higher in rank than the ordinary slave, for she had general supervision over the fifty female slaves of the household, and assisted the mistress in teaching them.[6] She also filled the important office of housekeeper,[7] was treated as a member of the family and was the friend and confidante of the mistress, who showed her great deference.[8] Penelope's nurse was also a trusted slave, devoted to her mistress.[9]

The historians have little occasion to speak of domestic life but we find mention made of a nurse in Herodotus.[10] This nurse is presumably a slave, for she received the commands of the parents to show the child to no one.

The nurses of tragedy were old women who had spent years in the service of their masters;[11] even after the child they had nursed had grown up, they were still retained in the household.[12] They, too, were slaves, and are spoken of as a "possession of the mistress," and "fellow slave." The fall of the mistress involved that of the nurse. Hecuba, bewailing her fate, foresaw that she who had once been the Queen of Troy, would be forced to become the nurse of children.[13]

It was not only captives and slaves who nursed children. In the fourth century we find at Athens free women performing the office of nurse,[14] and many free-born women compelled by stress of poverty to become nurses.[15]

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No instance is given by Plato or Aristotle of the manumission of a nurse. The nurse of new comedy was usually a slave,[16] still, she sometimes received her freedom "though emancipated, she yet remained in the service of her former master," her status being similar to that of the metic. We also have inscriptional evidence that women belonging to the metic classes were employed as nurses and received wages.[17]

Though the Athenians had a natural repugnance to the severity of the Spartan discipline, some of the Lacedemonian customs found ready acceptance in Athens. Aristophanes says that the Athenians were "Spartan-mad." For this reason, no doubt, Spartan women, whose robust health was famed throughout Greece, were often employed as nurses.[18] Nurses were also obtained from Corinth,[19] Phrygia,[20] and Thrace.[21]

Plutarch insisted that the nurse be selected with the utmost care, laying down as a fundamental qualification that she be of the Greek race.[22]

Such was the social status of the Greek nurse. We may conclude, then, that the nurse, though usually a slave, was sometimes manumitted, that a preference was frequently shown at Athens for the foreign-bred nurse, and that, on occasion, free women resorted to nursing as a means of gaining a livelihood.

DUTIES OF THE NURSE

Among the principal duties incumbent upon the nurse of an infant was the giving of the bath. We infer from several sources that it was given immediately after birth.[23] Some nurses preferred pure water; others, like the Spartans, bathed the child in wine, as a test of its strength, they being of the opinion that the weakly ones would faint, but the more vigorous would acquire firmness and hardness from a bath of this kind.[24] On a vase portraying the life of Achilles, one of the scenes shows the nurse giving the infant son of Thetis his first bath.[25]

Attica nurses wrapped the infant in swaddling clothes (sparguna).[26] As far as we can gather from the grave reliefs, these seem to have been long, narrow strips of cloth, bound like bandages around the child's body, which they completely covered from head to foot, leaving nothing but the face uncovered.[27] White, purple, and saffron are mentioned as colors of these bands. The practice of swaddling children is alluded to by Hesiod[28] and frequent reference is made to it by the tragedians.[29] The Theban children given over to the State were swaddled.[30] The nurse in the *Amphitryo* complained that Hercules was so large she could not swathe him.[31] How long the children were kept thus bound, we do not know, but we can hardly suppose that it was until they had reached the age of 2 years, as Plato advises.[32] In the third century, A.D., the child was swaddled from forty to sixty days, according to Soranus. The Spartan nurses dispensed with these swaddling bands, allowing the children to grow up unrestrained in limb and form.[33] Exposed children were sometimes recognized by the swaddling clothes.[34]

The child was suckled either by mother[35] or nurse.[36] Naturally, the practice of employing wet nurses prevailed chiefly among well-to-do mothers.

The author of *De Liberis Educandis* counsels mothers to nurse their own children, and enlarge upon the advantages accruing therefrom; nevertheless, he permits the employment of wet nurses wherever the mothers cannot perform the duty themselves.[37] Antiphanes considered the Scythians the wisest of men because they fed their children on mare's and cow's milk, and did not entrust them to nurses, as did the Greeks.[38] Plato refers to definite laws regarding the nurture of children and speaks of the time when they were fed with milk.[39] In the community of wives and children, he would have the mothers, from a feeling of humanity, assisted in the nurture of the children by nurses, "supplying other women, having good milk."[40] Aristotle associates infantile maladies with the physical condition of the nurse, "children are very subject to take convulsions, and more especially those who are very well fed, most of all when they use milk that is too rich, or the milk of fleshy nurses, who are too fat. Children cut their teeth more easily if their nurses have warmer milk."[41] He objects to the use of wine for the young children,[42] and deems it unsuitable for the nurses as well. "Wines are not profitable for the nurses."[43] Dion Chrysostom speaks of the use of wine, nurses' milk, and bread, for children.[44] Hippocrates says, "I hold it is better to give children only the most diluted wine, for such will not burn up and dry the veins."[45] After being weaned,[46] children were fed on milk[47] and honey.[48] According to Athenaeus, young children thrive well on the juice of figs.[49] They were also fed on morsels.[50] The practice of first chewing the food before giving it to the child seems to have been usual, for we have several allusions to it. Democrates likens the orators to nurses "who devour the morsels themselves, and leave the saliva for the children."[51] Nor did it escape the ridicule of Aristophanes who says "and like children's nurses, you grudge the food you give them. You champ and champ; and for one morsel that you give the child, eat three yourself."[52] Athenaeus tells the absurd story of a man who had his nurse chew his food for him all his life.[53]

In the beautiful idyllic scene of Illiad 6, 389 ff., where Hector bids farewell to Andromache and his darling son, it is to the familiar arms of the nurse that the child turns, when frightened by the glancing helm. "The child shrank, crying, to the bosom of his fair girdled nurse." "And when sleep fell on him, and he ceased from his childish play, then he would slumber softly nested in his nurse's arms, having satisfied his heart with good things."

The faithful Eurycleia carries Odysseus and lays him in the arms of his grandfather that the latter might choose for him a name.[54] The author of the Homeric hymn to Demeter puts these words into the mouth of the goddess nurse, "Well could I nurse a young child, carrying it in my arms."[55] The nurse in Herodotus VI carried the child each day to the temple of Helen.[56] Iphigenia, speaking of Orestes, says that she left him at home, a young child, in the arms of his nurse.[57] At the festival of the Amphidromia, it was the nurse who carried the child around the hearth;[58] and in the Nurse-festival (tithenidia) at Sparta, the nurses carried the male children to the temple of Artemis.[59] We know that nurses walked the floor with fretful children. A good instance is given in

Menander's *Samia* where an old nurse fondles a child to her heart's content, kissing it and calling it soft names, walking around with it until it is quiet.[60]

In a passage of the Laws, where Plato lays down rules for the management of infants, he advises that infants should be kept in perpetual motion, and live as if they were always tossing at sea. He compares the principle on which religious ecstasy is cured by a strain of impassioned music, with the method of nurses, who lull their babes to sleep, not by silence but by singing, and not by holding them quiet, but by rocking them in their arms.[61]

This perpetual motion used by the nurse is referred to in the Timaeus,[62] and Aristotle thinks "it is of advantage to have all the movements made (of the bodies of infants) that it is possible to have made in the case of creatures so young."[63] Plato lays down regulations for the nurses to carry the children into the fields, to the temples, and on visits to their acquaintances until they are able to stand alone. "We are, moreover, compelling the nurses, by legal fines, to carry the children either into the fields, or to the temples, or to their acquaintances until they are sufficiently able to stand alone . . . lest their limbs become distorted while forcibly resting upon them."[64] This is doubtless the reason why there is no mention made of a contrivance to keep the children's limbs straight like the Serperastra in use among the Romans.[65] The Greeks were careful to develop the body of the child to have it well shaped. The writer of *De Liberis Educandis* thinks it necessary for the members of children to be shaped aright, as soon as they are born.[66] In the *De Virtute*, Plutarch tells us that this is the work of the nurses.[67] Plato, speaking of the influence of stories on the minds of children, says, that we must persuade mothers and the nurses to form the souls of their children by these stories, "even more fondly than they moulded their bodies with their hands."[68] This practice continued down to the days of Galen, as is shown from the following, "The nurses of infants mould their limbs as if they were of wax."[69]

The nurses had various contrivances into which they placed the children after they were lulled to sleep. We read that Alomena cradled her children "within a brazen shield."[70] Military men were accustomed to place their children in shields after birth, that they might become vigorous and strong.[71] A specimen of a Greek cradle, that of the infant Hermes, a little, two-handled basket, shaped like a shoe, is seen on a vase.[72] Another kind of cradle (skaphe) is mentioned as being instrumental in the recognition (anagnorisis) of exposed children.[73] Children were also exposed in a cradle (skaphe).[74] The nurse of Zeus lulled him to sleep in a golden winnowing fan.[75] It was considered an omen of future wealth and prosperity to place children in these winnowing fans (likna).[76] Another kind of cradle looks like a bed on rollers and answers very well to the description given by Plutarch, "such easily moving little beds as are contrived for the children."[77] The rocking of the cradle is mentioned by Athenaeus, "the nurse put the child in the cradle and whenever it would cry . . . would rock the cradle and lull it to sleep."[78]

It was natural for the nurse to amuse the children with the various kinds of toys in use in antiquity. Of these, both the literature and the art of Greece

furnish many examples. The nurse sometimes made toys for the children; for example, the wonderful ball of Zeus, "which his dear nurse Adrastea made for him."[79] The shaking of rattles (krotala) was resorted to, we learn from Pollux,[80] and Stobaeus.[81] "The rattle and timbrel with which the nurses quiet the children." A vase painting shows a nurse dangling a fruit before a child.[82] Plutarch speaks of dolls,[83] and Vitruvius mentions a Corinthian nurse who adorned the tomb of her nursling with a basket of its toys.[84]

To keep the child clean and to attend to all its wants were the principal occupations of the nurse.[85] The fondling of children and the use of pet names were resorted to by the nurses.[86] Demosthenes acquired the nickname "lisper" (Batalos) from his nurse.[87] In learning to walk, the children must have had many a tumble, but the nurse was always at hand to pick them up and clean them, tidy their dress, and afterward to find fault and correct them.[88] Epictetus speaks of a nurse beating the stone which had caused the child to stumble.[89] Aristotle thinks that the crying of infants should not be restrained, as it is conducive to their growth,[90] but Plutarch says "as the nurse says to the child, 'don't cry and you'll be taken up.'"[91]

By means of amulets and charms the nurses sedulously guarded the children against the pernicious influence of witchcraft and the evil eye. "I will nurse him and never I ween through any heedlessness of his nurse shall witchcraft hurt him for I know an excellent safeguard against woeful witchcraft."[92] The amulets were usually of a grotesque character that the sight being diverted to them should not make so strong an impression on the child.[93] On the approach of a stranger, the nurse in charge of a sleeping infant would spit towards him, as if to keep off from the child a possibly evil influence.[94] Another charm against the evil eye is referred to by St. John Chrysostom, "The women in the bath, nurses and waiting maids, take up mud and smearing it with the finger, make a mark on the child's forehead and if one ask what meaneth the clay and the mud, the answer is that it is to turn away an evil eye, witchcraft, and envy."[95]

At what age the children left the care of the nurses is not certain. Chrysippus allows three years to them,[96] and according to Plato, the boys and girls were separated at six.[97] It seems clear that the boys, at least, were sent early to school to keep them out of harm's way. "The very nurses will tell you as much—children should go to school because even if they are not old enough to learn, they will at least be out of mischief."[98]

The tie between nurses and child might continue strong through later years. She often remained with the family as the attendant, and sometimes the confidante of the young maiden. Thus, Nausicaa's old nurse lights her fire and prepares her evening meal.[99] The same nurse who had attended Phaedra as an infant remained in her service until the death of her mistress.[100] We read that the nurse accompanied the young maiden out of doors and guarded her well, looking askance at admirers who were attracted to the girl's beauty.[101] She was sometimes the go-between in the maiden's love affairs,[102] she was wont to

comfort and console her charge when grown up, and we even have an instance that a nurse was consulted in an affair of State.[103]

Outside of Homer, we do not find the nurse as actively engaged in duties toward the grown son, as toward the daughter, but indications of the love and gratitude evinced by young men toward the nurse of their childhood is shown in the relatively large number of monuments and epigrams dedicated to them.[104]

When the nurse was not occupied with the child, she owed toward the household duties which are specifically mentioned in Homer but not so clearly defined in later authors. In Homer she was the mainstay of the house, having complete charge of the domestic arrangements.[105] The nurse of tragedy is occupied almost exclusively with the mistress,[106] and in comedy she seems to have authority over some of the servants.[107]

Instances of the love and devotion of nurses are not wanting in the literature. From Homer down we see the nurse as a kind mother, lavishing love and affection on the child that she nursed, and willingly giving her services to one who reminded her of her master.[108] A picture of true devotedness is given by Herodotas, where a nurse takes an ugly child every day to the temple of Helen to implore the gift of beauty for her charge.[109] It was the nurse who saved Orestes from his mother after his father's murder, and she was full of love and devotedness to the child.[110] Examples of tender attachment are also met in real life. Demosthenes says, "She had no kind of family connection with me except that she had been my nurse."[111] Neglect and unkindnesses are not characteristics of the Greek nurse, as popularly conceived. Of this, we have ample evidence of the number of metaphors employed in the literature, wherein the nurse figures, always in a good sense. One's fatherland is frequently called a nurse, since the care and nurture bestowed on a man by his country is like that given a child by his nurse. We read of the "much nourishing nurse, Greece,"[112] "Your motherland, the most beloved nurse,"[113] "This thy country nursed thee,"[114] and many others of a similar nature.

EDUCATION GIVEN BY THE NURSE

The importance of the nurse in Greek life may be judged from the fact that to her as well as to the mother is entrusted the early education of the child. Quintillian says, "Those advised better who like Chrysippus think that no part of a child's life should be exempt from education, for Chrysippus, though he has allowed three years to the nurses, yet is of the opinion that the minds of children may be imbued with excellent instruction even by them."[115] The same author wishes nurses to be women of some knowledge. At any rate, they should be the best that circumstances allow.[116] Plato says the nurse taught the children to distinguish between ordinary words. "Tell me, said he, Socrates, have you a nurse, because, said he, she overlooks your cold, and does not wipe your nose, and you learn from her neither sheep nor shepherd."[117]

The first lessons of the nurse were imparted by stories and songs. Plato advises mothers and nurses to mould the minds of the children by means of these tales.[118] In ancient literature we find only isolated traces of nursery tales,

though we have sufficient evidence to prove their existence, and suggest their character.[119] Nurses had many ways of acting on the imagination of their young charges in order to secure their obedience, to quiet them, and put them in good humor. The choice of the tales depended upon the nurse and the intelligence of the children, who were quieted by stories after being punished.[120] As a substitute for the sandal, which, according to Lucian,[121] was energetically applied, they sometimes told the children stories of an awe-inspiring character. The time-honored bogey was always in requisition to frighten them into good behavior, while there were tales of a pleasing character for the good children.[122] Of the bogey, the most frequently mentioned is Lamia whose children were destroyed by the jealousy of Hera. In retaliation, she killed the children of others. She was said to devour children alive. She is portrayed as a monster, hideous and deformed, hungry for human flesh.[123] Belief in her is so common in Greece that if a child dies suddenly they say Lamia snatched the child.[124] Acco, another bugbear, carried off naughty children in a bag[125] and the Empusa, or hobgoblin, could assume any form she pleased.[126] The wolf, too, had its place in the literature.[127] What the children preferred to these bogeys were the stories told to put them to sleep or to amuse them. The nurses had a store of such tales; "Nurses Tales" have grown into a proverb.[128] Plato enlarges upon the care to be taken in the selection of these tales,[129] and Plutarch thinks nurses should be restrained in the choice of these stories.[130] Aristotal wishes to place them under the supervision of the Paedonomoi.[131]

On the other hand, ancient mythology is so full of humor and imagination, so rich in amusing adventure that many of these same stories might do excellent service today as nursery tales, for example: the inventiveness of Hermes, even in his cradle; the adventures of Odysseus; the labors of Hercules; the magic rings of Timolus,[132] the ring of Gyges, which rendered its wearer invisible;[133] and others of a like nature would furnish enjoyment to many a child.

There was at Athens a store of popular tales for the amusement of children. Allied to the nursery tales are the lullabies of the nurses "as old as the world and which will last as long as the world."[134] They seem to have been simple melodies without words, sung to a certain rhythm.[135] Sextus Empiricus styles them a metrical humming. To these melodies the nurses probably adapted improvised words, as we do. This view is borne out by the fact that certain specimens exist which are imitations or elaborations of those really in use at the time they were written. The lullaby of Alcumena in Theocritus is an instance.[136] These are but traces of a class of songs without doubt employed by the Greek mothers and nurses to lull the children to sleep.

MONUMENTS TO THE NURSE

The relations between nurse and master were of that sacred character which ceased not with death. Her sincere and tender affection was not only repaid during life by the master's solicitude for her well-being, but after death her memory was frequently perpetuated by the erection of monuments. The unearthing of many of these has proved a fertile source of information concerning

the nurse. Her name, sometimes her parentage, and even details of her life and virtues, find expression in the sepulchral inscription.[137] In addition to these, we have literary evidence of other monuments in honor of the nurse.[138] In keeping with the true character of the nurse is Callimachus' epigram, wherein he commemorates the goodness of the Phrygian nurse, Aeschra, to whose memory her master set up her statue, in token of gratitude for her nurture.[139]

Thus, from the study of the inscriptions as well as from the literature, we learn that the Greeks had for those devoted women who stood to them in place of mother a tender attachment which often continued all through life; even after the nurse's death they sought to give some expression to it by writing epitaphs and erecting monuments to her memory.

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The Academy Study of Child Health Services

THE PURPOSES AND PUBLICATION OF STATE REPORTS

The facts which the Academy Study has been harvesting during 1946 are now, in 1947, ready for processing into something which should chart the future for both pediatrics as a specialty and for the child health program, the responsibility for which we share with fellow workers in child health throughout the country. The degree to which hospitals, health services, and practitioners in medicine and dentistry have supported our inquiry gives strong evidence of the esteem and trust with which the Academy is regarded. It is time we considered the probable nature of our findings and how the facts may be most effectively presented. This should be preparatory to an early definition of the policies for which the Academy stands and the development of a program for action.

In the November issue of THE JOURNAL OF PEDIATRICS, Dr. John P. Hubbard, the executive director of the study, described the interest which had been evidenced from many quarters in the publication of state reports and the steps which had been taken by the central office to get state chairmen and executive secretaries to share their experiences and varying points of view. It is now timely to discuss the purposes of state reports and some of the problems which will arise in the course of their publication.

The National Report of the Academy of Pediatrics will accomplish two important objectives:

1. It will provide a basis for appraising present-day pediatrics and determining how pediatricians will be trained and practice in the future. This is a matter of family interest to all members of the Academy.
2. It will provide data, supplementary to those already available, regarding facilities for the care of children, on the basis of which sounder local and national plans can be made for improving present health services. In this sense the national report can be considered a public service. It is understood that the report will not consider the question of standards. These will have to wait on future Academy action and policy decisions. First we must have the facts.

Although state reports will be narrower in scope, what they lack in breadth they should make up for in local interest. Action on a national basis may wait, but state reports should be written so as to be put to early use. They can serve the following purposes:

1. They will be of help to local medical and dental societies in showing the distribution of doctors and dentists and the contribution they are now making to child health.
2. They will provide information for the improvement of voluntary and public health programs. Too often the study is thought of as a means whereby only publicly supported health activities will be aided. Voluntary organizations such as community councils and community chests will profit equally from our work.
3. They can guide foundations and other sources of financial support in the expenditure of their funds.
4. They can provide valuable material to state groups interested in improved local services for children. There is a real need for information which will help doctors and health officials in their efforts to convince cities, towns, and counties that health work needs strengthening.

Pediatricians must consider what they wish to accomplish in terms of public service within the state and shape the state report to those ends. If objectives are less broad we shall be rightfully considered as narrow-minded and self-seeking.

The value of state reports will be proportional to the imagination and public spirit of the state chairmen and the Academy members in his state. It has been our experience

that an interest in public affairs, so much needed for the successful utilization of state findings, is more apt to be found among pediatricians in smaller towns and cities. Pediatricians in centers of population seem to feel less responsibility for children's health programs. There is a real need for men who are willing to look beyond the narrow circle of practice or hospital interests for a broader applications of their abilities. This seeming indifference to what the study can accomplish for the Academy is due to a preoccupation with clinical problems. Too many of us persist in viewing the medical scene through a microscope when a pair of binoculars would occasionally be more relevant.

There are certain misconceptions which contribute to this state of mind. Some pediatricians seem to feel that the medical needs in their state are already known. Others think that the academy has not made its motives for conducting the study sufficiently clear. There is, in some quarters, a suspicion that the Academy is being made the tool of government or even an agent of the income tax collector.

It is erroneous to assume that present information about our health services and programs is sufficient. In a state like Massachusetts its inadequacy is attested by the eagerness which various foundations and community councils have shown for facts by which to gauge their support of facilities for the care of children. In several instances they had independently gone in search of the facts. These agencies realize that voluntarily contributed dollars must be made to stretch to new limits and used only for the support of the most worthy enterprises.

It is interesting to see how meager information can be in regard to essential medical services. For example, in Massachusetts the bed capacities of a significant number of hospitals is unknown. Since they are not licensed, there is no official source for knowledge about their size, equipment, or the extent of the service they render to the public. Other obstacles to complete information are variations in the licensing laws by which institutions are under the control of various departments in the state government. Considering the diverse interests and responsibilities which governmental departments must assume, it should not be surprising that information is often so hard or impossible to obtain.

There is little collated knowledge about hospitals in terms of their capacity to give specific types of service. In instances where special control programs have been developed against pneumonia, prematurity, venereal disease, or infantile paralysis, the extent of available facilities is apt to be known, but there is no comprehensive idea as to their quality nor how well they are distributed.

Existing clinic services are pretty well known, but figures regarding the total service they give are not complete. The amount of care given to handicapped children is well defined for social security programs, but the contribution made in hospital out-patient departments is to a large extent concealed.

Practically nothing is known about the proportion of services to children rendered by practitioners, a factor which must be better estimated if any future planning is to be realistic. The dentists in the state realize that few of them treat children but, with the present interest in expanding dental health programs, it is essential that dependence be placed on more than guesswork.

Usually the number of pediatricians in a single state is not large and there are corresponding limitations to the scope of their activities. However, they can be important catalysts in any activities concerned with children. The state report is one of the means by which they can exercise this stimulation.

FORM OF STATE REPORTS

If state reports are to represent the Academy effectively they must be published in an attractive form and written so as to lead to well-considered action by public spirited professional and lay people. They need not be ornate, and in a rural state will necessarily be short and simple. For larger urban states with a variety of health services one should consider the possibility of two reports. The first should be a much simplified publication for general, professional, and lay consumption, which would headline the chief pediatric problems in the state, give the study findings, and make suitable recommendations for

their solution. The second could be a more lengthy report complete with tabulations for use by those with more technical interests. An average state will have to compromise between both types of report or separate the material presented so that the facts are not obscured by too many technical tables.

DISTRIBUTION OF STATE REPORTS

The next question to be answered is, "Who is to get the report?" The wider its distribution, the greater will be the informed public to whom we may look for intelligent support of our recommendations and any plans for their realization.

A distribution list should be drawn up and should usually include the following:

1. State medical society.
2. State dental society.
3. State board of health.
4. Foundations or other agencies contributing to the study.
5. Organizations in the state actively interested in the welfare of children. This should include community funds and councils.

All these agencies should be asked to indicate the number of copies they will want for distribution.

PUBLICATION OF REPORTS

In whose name will the state report be published? What will it cost? Will copies be distributed gratis or will they be sold for a nominal sum? These are all questions for the state chairman and his associates to decide.

In states where Academy members are limited it may be wise to develop a liaison with some organization already well known for its interest in the medical problems of the community and suitable as a co-sponsor of the report. This is already being done in several of the New England states.

The ideal person to write the report would be the state chairman or the executive secretary. In some states this responsibility has been entrusted to medical men qualified in pediatrics who will be using the material as the subject for a doctoral thesis. Whoever the author may be, he must work directly under the guidance of the committee making the state study or with a special report committee.

STATISTICAL MATERIAL

The statistical material used as a basis for the report will come from the central office. To this will undoubtedly be added information gathered from local sources. The material from the central office will in general be of two categories. A great deal of the information will be tabulated for the State as a whole and for special county groupings. These groupings are designed to show differences between urban and rural areas, different geographic divisions and health districts. In the second category will be detailed listings of data for individual hospitals, community health services and physicians and dentists in private practice for each county and city of 10,000 or more population. It is obvious that state chairmen will wish to have adequate consulting assistance in the interpretation of this material.

SUMMARY

Any state report will be effective in proportion to the enthusiasm and farsightedness of the pediatricians who have produced it. Local facts enlist local support and interest. If, as many of us believe, the difficulty with certain child health programs has been their failure to recognize the peculiarities existing in individual states, the remedy should lie in better defining them so that they may receive more suitable attention in the future. Strengthening of local health services must be based in large measure on better knowledge and utilization of local health resources. The Academy has already stated that the facts disclosed by the study will be made available to interested agencies in any state. The state report is the most important medium for accomplishing this purpose.

LENDON SNEDEKER, M.D.
Regional Consultant
New England Area

The Social Aspects of Medicine

COMMUNICATIONS

I have just received the letter from Dr. Donald Paterson of the Great Ormond Street Hospital, London, whom the readers of the JOURNAL all know by reputation and whom many know personally. The letter is full of the soundest comment and advice. Dr. Paterson's letter is of particular importance because medicine in England has been through much of what is at present threatened in this country, and is at present lying like the prisoner in "The Pit and the Pendulum," with the pendulum of State Medicine swinging nearer and nearer.

I do not know how Dr. Paterson got the idea from this column "that the U. S. A. is likely to be taking steps for a State medical service." As editor of the column, I never intended that any such impression should be created. I hope personally that some way may be found to develop a program for medical care which will be so superior to a State medical service for all concerned that the thought of the latter will be abandoned. What I have tried to reiterate and reiterate in the column is the necessity for pediatricians in this country to think—to think with completely open minds— and, in the light of the facts, to develop their own plan, the most intelligent and the best plan possible to meet the new, changed demands for medical care.

E. A. P.

27 Devonshire Place,
London, W.1.
7th January, 1947.

Dear Dr. Park:

When I read the column allotted to you in the JOURNAL OF PEDIATRICS, I feel that the U. S. A. is likely to be taking steps for a State Medical Service rather like the steps which have been taken and passed into law in this country. Being a Canadian, I hesitate somewhat to make any comments on what has taken place, but my English paediatric friends are much too wise to commit themselves, and leave such things to people like myself.

To start with, have no doubt in your mind that a state medical service, on paper, at least, is extremely popular with the public, and is backed by both the present Government and the opposition, although they may differ about some details. One meets very few people indeed among the lay public who are not entirely enamoured of it. The trouble will be to work out a successful scheme, but unless that is done quickly it will be too late. There are very few thinking doctors who would not agree that a doctor civil servant would be much less efficient than one not in the State service. Medicine does not lend itself to bureaucratic control. If you read Wallgren's description of state medicine in Sweden in the December number of the *Canadian Medical Journal*, you will see that it is only a partial state medical service which is supplied, and the Swedish have "stood out" against full-time service. It is my experience that only a very few, very exceptional, individuals remain efficient on a full-time salary in medicine.

The terms of payment to doctors in this country have not yet been made known; for instance, we don't know whether practitioners will be paid per capita, as in the present National Health Service, or by salary, or partially in both ways. It is not possible to say what "plums" are to be offered to the profession.

In paediatrics I think every one would agree with me that the service offered the public in large cities and near university centres is excellent; it will improve over the years, but it has already attained a very high standard, and both the poor and the rich are catered for. It is in the more sparsely populated districts, where the hospital facilities are poor and the medical profession is overworked and ill-equipped, that the public suffers. In this country this was very clearly seen and realised during the war. Throughout the war period, children were evacuated from all the large cities to the surrounding country districts and

into the remote parts of Scotland and Wales. With them went the children's hospitals, the nurses, and the paediatricians. The country folk were delighted, and maintained that they had never had such medical care before. Naturally, they would like to continue this in the future. The problem is to induce the right young men and women, highly trained and ambitious, to go to these less attractive areas; there is no use offering them an increase in salary alone; they require improved hospital facilities in order to do good work; their wives and children will not be happy and satisfied unless there are educational facilities and some modicum of culture and comfort. Under a rigid state medical service, a young man could be drafted to such an area and required to stay there indefinitely, as he would in the army; we would not like to see this happen, I am sure.

Now what should one do to prepare for these inevitable changes which the public demands? I feel sure that a survey of the situation, such as I gather Colonel Hubbard is preparing for you, is certainly the first step. The magnitude of the problem is then quite clear. It seems that to attract a young man to an unattractive district, one must keep him constantly in touch with some teaching hospital; a state might well therefore be divided into regions, centered on a university. If this were kept constantly in mind, throughout the survey, it might save much labour later. In these days of modern travel, a journey of fifty or more miles on one or two days in the week to do outpatient sessions, give lectures, or make ward rounds, in a teaching hospital is not an impracticable possibility. The linking up of preventive and curative medicine in the same individual seems to us inevitable, and the school clinics and infant welfare centres should be part of the local paediatrician's duties.

I happen to be one of the people who think that there is great strength in lack of uniformity. To have a great variety of experiments in bringing about this change, and adapting methods of finance and staffing to different situations, seems to me much wiser than trying to lay down a rigid arrangement for a whole country. This tight little island with its short distances, easy communications, and dense population lends itself much better to a uniform state medical service than would the U. S. A.

Once the problem is explained to the paediatricians and they have had a survey of their own area showing what the state of affairs is at present, both as regards beds and personnel, but, much more important, showing what is required to set it right, then the medical profession must make its effort.

It seems to me inevitable that help must be sought from Federal, State or municipal authorities, particularly for capital expenditure.

If you have the hospitals right for a start, a great part of the success of your efforts is assured.

How clever the Swedish were in the constitution of their council to direct the whole affair. This is composed of doctors from the universities and not from a Ministry of Health.

When I read the article by Wallgren and noted the very small salaries received, I wondered if the doctors were realising their hopes and ambitions and were really happy.

Lord Dawson of Penn besought the profession in this country on many occasions to bring in state medical services slowly, bit by bit, as it is something which, once done, can never be undone. We earnestly hope that this tremendous experiment of "buttering" the brains and talents of the medical profession in a very thin layer over the whole of the country, rather than in a few large cities, as at present, will be a tremendous success.

Kind regards,

Sincerely yours,

(Signed) DONALD PATERSON, M.D., F.R.C.P.

December 4, 1946

Dear Dr. Park:

Elsewhere in this journal I have contributed a paper which outlines the scope and aims of developmental pediatrics.* By developmental pediatrics we mean a form of clinical medi-

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From The Clinic of Child Development, Yale University.

*See page 188.

cine which is especially concerned with the diagnosis and supervision of child development. This phase of pediatrics has vast implications for the social aspects of medicine. I, therefore, venture this informal letter addressed to your editorial department.

We can discuss the subject without entering too deeply into the controversial issues of social legislation, but if a developmental type of pediatrics is destined to become a major feature of clinical medicine, it is not too early to consider problems of professional training. Adequate personnel is as important as adequate legislation. Fortunately, the survey of current pediatric education bids fair to become one of the most valuable features of the Academy's Study of Child Health Services. The Board of Pediatrics has been placing increasing emphasis on the field of growth and development. How can this emphasis be implemented through medical schools and hospitals? In a word, how can developmental pediatrics be brought more squarely into the scheme of pediatric education?

For the sake of discussion, I suggest that the study of child development be raised to the status of a clinical subject, with basic theoretical instruction concretely related to the clinical manifestations of normal and abnormal growth and development. This objective cannot be realized simply by adding a new subject, entitled Growth and Development, to the curriculum. Both at the undergraduate and graduate levels medical teaching needs to be correlated around fundamental themes.

For the pediatrician the fundamental center of correlation is the child as a unitary organism. To further this correlation, various fields of instruction can be focussed more definitely on the life cycle of the child, using the normal progressions of this cycle as a basic frame of reference. It is the growth cycle which gives unity to the child and which integrates the three panels of his development, the anatomic, physiologic, and behavioral. When the study of these panels is pursued too independently, instruction tends to become disjointed. To be sure, the task of correlation falls in some measure on the student, but it is a complicated task and the medical schools should assist him from the beginning to acquire an integrated outlook on the whole field of child development both in its normal and pathologic aspects. We need reorientations in medical instruction more than we need change of content. These reorientations can be accomplished by converging diversified avenues of approach upon central themes.

If development is consistently made a central theme, there are few subjects in the field of pediatrics which cannot in some way be related to factors of age and developmental maturity. A developmental approach might bring an answer to the often repeated question, Why do we teach embryology at all? The status of embryology in many schools is still somewhat undefined, if not anomalous. Embryology, however, becomes truly a basic medical science in any program of pediatric education which concentrates on the processes of child development. We must, however, adopt Huxley's point of view and give equal weight to the postnatal and prenatal aspects of human embryology. Broadly conceived, embryology includes physiologic functions as well as anatomic structures. Moreover, there is an embryology of behavior and the whole organization of the child's development can be envisaged in terms of a dynamic developmental morphology. We might also remind ourselves of Adami's wise remark that development is a process every whit as real as secretion.

The educational problem is to make this elusive process real to the student by using all possible concrete methods at our disposal. Perhaps we need an integrating textbook which will bring the anatomic, physiologic, and behavioral manifestations of growth and development into closer correlation. But even a good book can be vitalized only by contact with concrete, illustrative infants and children. The teaching task is to take the whole subject out of the academic mist and to impart a lively clinical appreciation of the stages and patterns of child development.

In our own field of developmental diagnosis, I think we have demonstrated the feasibility of concrete, intimate instruction both at undergraduate and at postgraduate levels. In addition to a basic text, we have used the following procedures: (a) self-instruction films; (b) observation (with discussion) of developmental examinations of normal infants of varying age; (c) observation and case studies of a wide diversity of developmental defects and deviations, examined on an active diagnostic service; (d) graduated participation and prac-

tice in the application of the diagnostic tests and norms. Brief comment may be made on these several methods.

The self-instruction films delineate the characteristic behavior patterns of infants at advancing ages. The student examines these films in precisely the same manner that he studies his histologic slides. By means of a personal desk viewer, under his own control, he examines the patterns of behavior, and associates them with a given level of maturity, 16 weeks or 40 weeks as the case may be. The basic films chart the normal progressions of behavior. He can study defects and deviations in the same manner. This method makes behavior as organic and as tangible as tissue. Child development is thus made a little less elusive.

But visual instruction must be supplemented by demonstration of the living, growing infant. For this purpose we arrange a series of developmental examinations of normal babies at progressive ages. The student witnesses the examinations from behind a one-way vision screen. Conferences follow immediately; they lead to comparative, systematic discussions, because the diagnostic examinations of behavior were made with a standardized technique which exposes the lawful sequences of development. Through such systematic presentation we can raise the study of normal child development to the status of a clinical subject.

The significance of normality is enhanced by similar contact with retarded, atypical, disturbed, damaged, and defective infants. Our diagnostic service provides a plentiful array of these conditions of maldevelopment. They are examined by the selfsame standardized methods employed with normal infants. Many of these infants have been repeatedly examined at earlier ages. This doubles and deepens the developmental perspective. The child, in conference, is not only compared with the normal maturity norms; he is compared with his previous self (often with previous cinema records to document the evidence). So again a comparative, normative approach serves to give reality to development as a process.

For the postgraduate physician who has already served an interneship in pediatrics or neuropsychiatry, we provide a specializing externeship of one or two years in duration. After an induction period of observation and of laboratory study of the self-instruction films, he is initiated into actual examinations of normal infants. As he develops skill and confidence he is given increasing responsibility with the cases admitted on the diagnostic service. He soon discovers that the behavior tests are not as simple nor as automatic as they may have appeared. He begins to respect them as diagnostic tools, which must be applied with finesse, and which become effective only as he can bring a fund of clinical experience critically to bear.

In this way he arrives at a medical outlook upon the everyday and the unusual problems of child development. The term development has now become less abstract for him. He thinks in terms of norms and patterns of maturity, of growth trends and growth capacities. He envisages the infant and child as a growing organism, whose mechanisms of development are not altogether past understanding, diagnosis, and supervisory guidance.

We know of no other way in which clinical and teaching personnel can be adequately prepared for responsibilities and leadership in the field of developmental pediatrics, a field which may well become a subspecialty recognized as such by a board of certification. Both in private practice and in public health organization there is bound to be an increasing emphasis upon a supervisory type of clinical pediatrics which will include normal as well as sick, defective, and handicapped children. To meet these mounting social demands, there will naturally be reorientations and perhaps even a mutation or two in the evolution of pediatric education.

At any rate, the current survey of the Academy invites consideration of the fundamental problem of professional training.

Sincerely,

ARNOLD GESELL

Director, The Clinic of Child Development,
Yale University School of Medicine
New Haven, Conn.

Academy News and Notes

NOTICE

Due to the increased cost of running the *American Board of Pediatrics*, the board has found it necessary to raise the application fee to $125.00, effective May 1, 1947.

The following Fellows of the Academy have been released from military service:

Charles E. Abbott, Tuscaloosa, Ala. *(Army)*
Robert D. M. Cunningham, Stamford, Conn. *(Army)*
Francis C. McDonald, Boston, Mass. *(Navy)*
William B. Nevius, East Orange, N. J. *(Army)*
Charles A. Tompkins, Omaha, Neb. *(Army)*

Dr. H. Harris Perlman, a Fellow of the Academy, has been certified by The American Board of Dermatology and Syphilology. He is the first pediatrician to be so certified.

News and Notes

THE FIFTH INTERNATIONAL CONGRESS OF PEDIATRICS

The Fifth International Congress of Pediatrics will meet in New York City at the Waldorf-Astoria, July 14 to 17, 1947.

July 14 has been set aside for registration, for the first plenary session of the congress and for the viewing of the exhibits. The opening session of the congress will be held Tuesday morning, and will be followed immediately by the first of the scientific sessions of the congress which will continue through Thursday. A telephonic translation system will be installed that will do away with the loss of time of translation into the various languages and make possible the presentation and discussion of more topics.

Dr. Rustin McIntosh of New York, chairman of the Program Committee, has consulted with the various national committees in arriving at the following outline:

I. Major Topics
   1. Diseases caused by filterable viruses.
   2. Chemotherapeutic agents in the control of infectious diseases.

II. Subsidiary Topics
   1. Neonatal mortality
   2. Incompatibility of blood.
   3. Alimentary toxicosis.
   4. Bio-immunologic procedures.
   5. Congenital heart disease.
   6. Rheumatic fever.

III. Sectional meetings

One session only will be given over to sectional meetings grouped under:

1. Factors in pregnancy affecting the child.
2. Future of preventive pediatrics.
3. Vitamin requirements and avitaminosis.
4. Nutrition.
5. Control of airborne infections.
6. Tuberculosis.
7. Endocrinology.
8. Insects and other vectors of infectious diseases; methods of control.

No simultaneous translation service will be available for these meetings.

The Exhibit Committee, under the cochairmanship of Dr. F. T. Mitchell, 376 S. Bellevue Blvd., Memphis 4, Tennessee, and Dr. F. F. Schwentker of Baltimore, is preparing a very extensive and comprehensive exhibit illustrating the advances in all fields of medicine, as well as in the general field of clinical pediatrics. One room will be set aside for movie demonstration. The scientific exhibit will represent the major contribution of the United States to the scientific program of the congress. Dr. Mitchell is very anxious to have all suggestions of available and suitable material sent to him at the earliest moment.

The Committee on Local Arrangements, of which Dr. Miner C. Hill of New York is chairman, has been given to understand that the hotel situation has eased up considerably and there is every prospect that it will be better next July. As soon as possible, special notices will be sent out to pediatricians regarding hotel reservations, and more details regarding program, exhibit and entertainment.

Trips to various medical centers are being planned by the committee on post congress tours in collaboration with the American Express Company, the travel agents for the congress.

The Organization Committee, composed of members from the American Academy of Pediatrics, the Pediatric Section of the American Medical Association, the American Pediatric Society, and the Society for Pediatric Research, wishes to call to the attention of each pediatrician that he can contribute greatly to the success of the undertaking by his attendance at and support of the congress. It is the hope of the committee that every American pediatrician will welcome this opportunity to act as host to the guests from foreign lands.

The sponsoring committee is as follows: Dr. Isaac A. Abt, Chicago; Dr. Amos U. Christie, Nashville; Dr. Hugh Chaplin, New York; Dr. Wilburt C. Davison, Durham; Dr. Adolph G. DeSanctis, New York; Dr. Martha M. Eliot, Washington; Dr. Lee Forrest Hill, Des Moines; Dr. Rustin McIntosh, New York; Dr. Edwards A. Park, Baltimore; Dr. Francis F. Schwentker, Baltimore; Dr. Clement A. Smith, Boston; Dr. Philip M. Stimson, New York; and Dr. Joseph Stokes, Jr., Philadelphia.

The officers are: Dr. Henry F. Helmholz, President; Dr. L. Emmett Holt, Jr., General Secretary; and Dr. Donovan J. McCune, Assistant Secretary and Treasurer.

CITIZEN ACTION FOR CHILDREN URGED BY NATIONAL COMMISSION ON CHILDREN AND YOUTH AT FIRST CONFERENCE

Adoption of an eleven-point action program for 1947-1948 led the list of important decisions reached by the National Commission on Children and Youth at its first annual meeting held in Washington, D. C., Dec. 9 to 11, 1946.

Successor to the National Commission on Children in Wartime, this new Commission was formed in February, 1946, "to give national leadership to efforts throughout the country to provide improved opportunities for children and youth." Its members include leaders of national organizations supporting programs for children and youth, representatives of professional groups, and state and local officials working in the fields of child health, child welfare, education, recreation, and youth employment. Leonard W. Mayo, Dean, School of Applied Social Sciences, Western Reserve University, is chairman, and Edith Rockwood, United States Children's Bureau, is secretary.

Reaffirming its position that it supports no specific piece of legislation, the Commission phrased its action program in terms of basic objectives to work for through public and private channels, in the fields of social security, health, education, welfare, recreation, youth employment, state and community planning, youth participation, and international programs.

A 1950 White House Conference on children and youth received the unanimous endorsement of the members who voted that such a conference should be broadly representative and supported, so far as possible, from public funds. It was urged that both the National Commission and similar state bodies be closely identified with the planning of the White House Conference, and the programs of popular education to stimulate state and local interest in it be conducted in advance throughout the country.

Other measures adopted at this commission meeting, which was attended by sixty-two members coming from a wide range of professional and citizen groups and public agencies, twenty-four representatives of seventeen state planning commissions for children and youth, and fourteen advisers from as many Federal agencies included the following:

1. Recommendations on increasing and extending the commission's work with professional, civic, and public groups; on strengthening its relations with state planning commissions, and with public and private agencies serving children and youth in the United States Territories.
2. Commendation of the President of the United States for his directive making possible the admission into this country of unaccompanied displaced children from Europe, and requesting the United States Children's Bureau to explore appropriate ways and means for increasing the number of children to be brought to the United States.

3. Creation of subcommittees of the commission to work with various federal interagency committees on youth employment and education, migrant labor, health programs for school-age children, and with the President's Committee on Civil Rights.
4. Study of the reports growing out of the Attorney General's Conference for the Prevention and Control of Juvenile Delinquency.

These and other recommendations adopted by the commission grew out of three half-day discussions centering on the questions:

How can issues be resolved in order to get action?

How can support of citizens in behalf of children and youth be enlisted through state commissions for youth and national organizations?

Urging the "mobilization of all possible resources as promptly as possible" for aid to children of other nations, the commission endorsed the International Emergency Children's Fund of the United Nations. It expressed its approval of the organization of the Social Commission of the United Nation's Economic and Social Council, and its hope that the Social Commission will establish promptly a subcommission on child welfare. Commission members were urged to study and make better known the programs affecting children developed by UNESCO, the International Labour Office, the World Health Organization, and the Food and Agricultural Organization. An exchange of experts and training of personnel between the Philippine Commonwealth and the United States was recommended as well as the extension of cooperative information and training programs between the American Republics. The United States Children's Bureau and Office of Education were asked to work out child health, welfare, and education programs for children in United States-occupied Pacific areas. The commission gave its encouragement to the efforts of voluntary organizations to aid distressed children and families around the world.

Invited together for the first time since their organization, the representatives of seventeen state planning commissions and councils on children and youth participated in the commission's group discussion sessions and held two sessions of their own. The exchange of experiences which came out at these meetings showed the widespread and lively interest on the part of the states in extending services and protections for children and youth. The group recommended that their organizations be recognized as appropriate state bodies to determine the action that should be taken on the Attorney General's juvenile delinquency conference, and that the United States Children's Bureau assist such state organizations in their work by drawing up a statement of principles, standards, and methods of work.

Members of the Commission were welcomed by Watson Miller, Administrator, Federal Security Agency, and Arthur J. Altmeyer, Commissioner for Social Security of the Federal Security Agency.

NATIONAL COMMISSION ON CHILDREN AND YOUTH ACTION PROGRAM FOR 1947 AND 1948

To conserve the gains that have been made and to go forward toward the achievement of its purposes in behalf of all children and youth, the National Commission on Children and Youth has adopted the following action program for 1947 and 1948:

1. *Extension of Social Security Programs Affecting Family Income.*—

   To seek increased coverage and benefits under social insurance, public assistance programs, or by other benefits.

2. *Expansion of Federal and State Cooperative Programs for Child Welfare.*—

   To press for Federal and State legislation that makes possible achievement of a comprehensive program of child welfare services, within broad programs of public welfare, available in every state.

   To work for better protection of the rights and welfare of children and youth through State legislation, such as laws relating to adoption, guardianship, illegitimacy, juvenile delinquency, and other aspects of child welfare.

3. *Expansion of Federal and State Cooperative Programs for Maternal and Child Health.*—

To press for Federal and State legislation that makes possible the achievement of complete health and medical care services for all mothers and children in every state, including services for crippled children.

To press for Federal and State legislation that will make possible the development of health services for school children through joint action by school and health authorities.

4. *Expansion of Mental Health and Guidance Programs for Children.*—

To work for the inclusion in health, education, and welfare programs of mental-health and guidance services for children and youth at all stages of their development.

5. *Federal and State Aid to Education.*—

To press for Federal and State financial aid to public education that will make fully available educational opportunity for all children from nursery school through high school, adapted to individual capacities and the special needs of each child.

To insure for all youth, regardless of their economic status, full access to advanced liberal, technical and professional education, in accordance with their interest and capacities.

To extend and improve all school services essential to the development of a rounded school program.

6. *Recreational Opportunity.*—

To work for the development of recreational services and facilities as a public responsibility, with Federal and State advisory services on community recreation programs.

To encourage planning for recreation by public and voluntary agencies directed toward services to all children and youth, and particularly to areas which have not yet developed such services.

7. *Improved Child Labor Legislation.*—

To press for extension of the child labor provisions of the Fair Labor Standards Act to cover all employment in or in connection with interstate commerce, including industrialized agriculture.

To raise standards of State legislation to set: a 16-year minimum age for any employment during school hours and for work at any time in manufacturing and mechanical establishments; a 14-year minimum for other employment outside of school hours; a maximum of 40 hours a week and no night work.

To extend compulsory school-attendance laws to cover all children between 6 and 18 years of age, with allowance for legal employment of those 16 and 17 years of age and exemption of high school graduates.

8. *Employment Opportunities.*—

To work for expansion of public employment facilities for counseling and placement of young people, to be developed in close relationship with schools and other community agencies.

To urge the inclusion of work opportunities for youth in public planning for full employment.

9. *State and Community Planning for Children and Youth.*—

To extend and strengthen state and community committees planning for children and youth on a continuing basis.

To obtain advisory service and assistance for such committees from the Children's Bureau and other Federal agencies.

10. *Youth Participation.*—

To encourage the cooperation of youth groups in the planning and development of community services on which they can make a contribution.

11. *International Programs.*—

To encourage, through the United Nations and other appropriate organizations, international action that will strengthen services for children and youth.

Dr. R. E. Dyer, Director of the National Institute of Health, United States Public Health Service, Federal Security Agency, on Jan. 5, 1947, issued the following statement on the use of glycols and ultraviolet radiation in the control of air-borne infections, to answer numerous inquiries from the public:

> During the past few months, several articles have appeared in the public press relative to the possible efficacy of glycol vapors and ultraviolet radiation in reducing certain infectious diseases, particularly upper respiratory diseases, such as the common cold. Due to the fact that many inquiries have been made as to the possibility of using one or both of these methods in public buildings, it is felt that a statement at this time should be made concerning the use of such installations.
>
> Committees of the National Research Council and the American Public Health Association have studied and reviewed the data on such installations. Within the past several weeks, these two Committees separately have submitted reports. Both of these Committees feel that the use of either glycol vapors or ultraviolet radiation is still purely in the experimental stage, and that the data collected so far do not warrant the installation of such equipment in public buildings and industry in the hope of cutting down upper respiratory infection. The U. S. Public Health Service, through its research organization, the National Institute of Health, has conducted rather extensive studies on both glycol vapors and ultraviolet radiation, and fully concurs in the reports and recommendations made by the Committees of the National Research Council and the American Public Health Association. It must be emphasized that direct, unshielded ultraviolet radiation of sufficient intensity to kill microorganisms in the air is also harmful to the eyes and exposed skin of humans. These observations are not intended to indicate that the future will or will not disclose new public health values in the application of either glycols or ultraviolet radiation. Much experimentation is needed, however, before a decision can be made as to whether such application may or may not be warranted.

Correspondence

London, England
December, 1946

I think you may like to hear of the interest in and emphasis on child health and well-being over here, as reflected in the recent establishment of professorial chairs in child health during the past twelve months. At the end of 1945, a professorship in child health was endowed in London by the Nuffield Trust, and Dr. Alan Moncrieff was appointed to this chair.

Since then the Universities of Leeds and Sheffield have both created professorial appointments in this subject. The establishment of these new professorships in such quick succession after the close of the war stresses the importance attached to this subject in England at the present time.

A link-up between the care and study of the sick child on the one hand, and the pediatric work, chiefly preventive, of the health departments of the public local authorities on the other, is envisaged in these schemes, the intention being to coordinate all pediatric work, and to bring into harmonious relationship the activities of the hospital physicians and consultants, the family doctors, and the public health departments.

Professor Charles McNeil of Edinburgh has just retired from the Chair of Child Health, and has been succeeded by Dr. Richard Ellis, who worked some years ago for a considerable time in the Department of Pediatrics of Harvard University, under the late Dr. Kenneth Blackfan.

Discussions concerning the proposed National Health Service have been continuing throughout the year, and now the broad provisions for such a service have been entered on the statute book. It remains, however, to hammer out the details. With this in view the British Medical Association arranged a plebiscite. Every member of the medical profession was requested to fill out a voting paper stating simply whether or not he was in favor of negotiating on this matter with the Government. A negative answer is to be regarded as implying also that whoever records it will not enter a health service based on the present outlines. The result of this plebiscite has just been published, and it shows a small majority in favor of refusal to negotiate on the act as it stands at present.

Inasmuch as the provisions for a unified hospital service are, on the whole, satisfactory, roughly 50 per cent of the consultants and specialists are not averse to the act, and the fact that the control of the hospitals is planned to be under the Ministry of Health rather than local authorities, is welcomed generally. At the same time the general practitioners, still the backbone of the profession in this country, are far less pleased with the service in its present outlines as it affects them, since they see in it a threat to their professional freedom. It is apparent, therefore, that an unfortunate split of opinion has occurred among the members of the medical profession itself.

What the exact outcome will be is not possible to say at present, but it seems quite clear that National Health Service in some form will be introduced in this country, although the details have yet to be determined.

The annual meeting of the British Paediatric Association was held at Rugby again this year, and was a great success. We had the pleasure of welcoming Dr. S. W. Clausen of Rochester, N. Y., who was then visiting this country. It is always most agreeable to have pediatricians from other countries as our guests at such meetings. An abstract of the proceedings may be found in the *Archives of Disease in Childhood*, 1946.

Our diet in this country is still restricted and tends to be monotonous, but there is no doubt that it is entirely adequate, and it is not often that one sees evidence of malnutrition. We hope that the food situation will soon improve, but no critical pediatrician expects to find any falling off in the nutrition of children, whose condition during the war remained so remarkably good. In this connection it is interesting to note that Magee, in his Milroy Lectures in 1946, makes the following statements, which are undoubtedly correct:

"The public health, so far from deteriorating *(during the war)*, was maintained and in many respects improved. The rates of infantile, neonatal, and maternal mortality and the still-birth rate reached the lowest levels ever. The incidence of anaemia declined, the growth rate and the condition of the teeth of school children were improved, and the general state of nutrition of the population as a whole was up to or above pre-war standards."

We are very interested in the projected International Pediatric Congress to be held in the United States in July, 1947. All of us would like to come, but on account of transport difficulties your correspondent feels that few British paediatricians will, unfortunately, find themselves able to attend.

KENNETH TALLERMAN.